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APRIL 1955

ABSTRACTS CONTENTS · APRIL 1955

COLLECTIVE REVIEW

A HALF CENTURY OF EFFORT TO CONTROL CANCER. *George T. Pack, M.D., F.A.C.S., and Irving M. Ariel, M.D., F.A.C.S.*, New York, New York 309

ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

Head

Surgical Treatment of Tumors of the Jaw; Indications for Endobuccal Resection. JORGE MARSILLAC 353

Eye

Blepharoptosis; A General Consideration of Surgical Methods; with the Results in 162 Operations. CARL CORDES JOHNSON 353
Surgery of Carcinomas in the Region of the External Palpebral Commissure. JOSÉ CONDE and ARTUR PINA 354
Metastatic Carcinoma of the Choroid. OLGA SITCHEVSKA 354

Nose and Sinuses

Olfactory Esthesioneuroepitheliomas of Louis Berger. L. FRUEHLING and CHARLES WILD 354

Mouth

Plastic Operations for Partial or Total Losses of the Lip. EDUARD SCHMID 355
Restoration of Lip Contour Using Fascia, Tendon, and Dermal Grafts; Correction of Flat Lip Deformity. KENNETH PICKRELL, FRANK MASTERS, NICHOLAS GEORGIADE, and CHARLES HORTON 355

Neck

Present Trends in Treatment of Carcinoma of the Larynx. R. G. MACBETH 355
Bilateral Neck Dissection with Excision of Both Internal Jugular Veins, and Related Matters. (Correction). E. S. MEYERS 356

SURGERY OF THE NERVOUS SYSTEM

Brain and Its Coverings; Cranial Nerves

The Treatment of Hydrocephalus. DONALD D. MATSON 357
Cerebral Angiography in the Diagnosis of Intracranial Lesions. OSCAR SUGAR 357
The Pathology of Spontaneous Intracranial Hemorrhage. DOROTHY S. RUSSELL, M. A. FALCONER, DIANA J. K. BECK, and W. H. MCMENEMEY .. 357
The Treatment of Ruptured Intracranial Aneurysms. WALLACE B. HAMBY 358
Cerebellar Astrocytomas. S. OBRADOR ALCALDE .. 358
Some Factors Which Affect the Value of Carotid Angiography in the Diagnosis of Brain Tumor. ERNEST H. WOOD 409

Spinal Cord and Its Coverings

The Value of Radiation Therapy in the Management of Intrinsic Tumors of the Spinal Cord. ERNEST H. WOOD, ALFRED S. BERNE, and JUAN M. TAVERAS 410

Peripheral Nerves

Peripheral Nerve Injury. BARNES WOODHALL 359

Miscellaneous

Pelvic Pain Based on a Vascular and Autonomic Nervous System Disorder. HOWARD C. TAYLOR, JR. 383
Malignant Hypertension Supervening Rapidly on Pre-Eclampsia. T. B. COUNIHAN and IL DONIACH 384
Experimental Allergic Encephalitis in Animals, and Its Bearing Upon the Etiology of Neuroparalytic Accidents Following Antirabies Treatment in Man. GEORGE A. JERVIS 405

SURGERY OF THE THORAX

Chest Wall and Breast

The Fascia of the Breast and Axilla. E. S. MEYERS. 360
The Technique of Extrafascial Radical Mastectomy. HUGH R. G. POATE 360

Trachea, Lungs, and Pleura

The Surgical Treatment of Patent Ductus Arteriosus; a Review of 50 Cases. IRENE S. CADE ... 360
Reduction of Pulmonary Reserve; Technique for Reducing Pulmonary Capacity to 15 Per Cent, with Measurement of Right Heart Pressures

and Arterial Blood Oxygen Saturation in Dogs at Rest and During Exercise. A. Flores, W. E. Adams, and J. F. Perkins, Jr. 360
The Surgical Treatment of Bronchial Asthma by Modified Operative Procedure. J. Daniel Szokodi 361
The Tubercle Bacilli in Pulmonary Lesions After Treatment by Chemotherapy and Excision; Study of 97 Cases. G. Canetti, R. Israel, P. Hertzog, P. Daumet, and L. Toty 361
Resection of Bronchus and Bronchotracheal Anastomosis in Tuberculous Bronchial Stenosis; Report of a Case. Cl. Crafoord, V. O. Björk, and H. Hilty 361
Local Treatment of Acute Pulmonary Abscess. E. Bauer 362
Lipoid Granuloma of the Lung. Rollin A. Daniel, Jr., and Thirwell M. Nolen, Jr. 362
Changes in Shape and Site of Intrathoracal and Extrathoracal Organs After Pneumonectomy, and Their Clinical Significance. M. Wenzl and E. Strahberger 362
Thoracoplasty; a New Osteoplastic Technique. Viking Olov Björk 363
The Study of Mitral Regurgitation by Roentgen Kymography; with Observations on the Movement of Cardiac Calcifications. Victor A. McKusick 409
Blood Groups in Carcinoma of the Lung. R. B. McConnell, C. A. Clarke, and F. Downton. 411

Heart and Pericardium

The Surgical Problem of Mitral Insufficiency. P. Chalnot, R. Benichoux, and C. Chardot ... 364
Results of Surgical Treatment of Mitral Stenosis. G. Dussaillant, J. Allamand, W. Sunkel, A. Del Valle, and R. Carrasco 364
Intracardiac Thromboses. Roger Letac, Robert Camain, Pierre Barroux, and Bruno Denis .. 365
Hypothermia as an Adjuvant in Cardiovascular Surgery; Experimental and Clinical Observations. H. William Scott, Jr., Harold A. Collins, and John H. Foster 365
Experimental and Clinical Observations on the Closure of Cardiac Septal Defects. Harris B. Shumacker, Jr. 365
The Obscure Physiology of Poststenotic Dilatation; Its Relation to the Development of Aneurysms. Emile Holman 366
Natural History of Aneurysms of the Aorta. John J. Granley, Louis G. Herrmann, and Rosamunde M. Preuninger 367
The Surgical Treatment of Coarctation of the Aorta. R. Milnes Walker and Herbert Haxton 368
Tolerance of Adult Rats to Profound Hypothermia and Simultaneous Cardiac Standstill. Suad A. Niazi and F. John Lewis 412

Esophagus and Mediastinum

Simple Stricture of the Esophagus. E. C. Mekie .. 368
Abnormal Ring Contractions of the Thoracic Esophagus; with an Account of Familial Manifestations. T. V. L. Crichlow and H. J. Shaw. 369
Esophageal Hiatus Hernia; a Clinical Study Based on 138 Cases, of Which 96 were Treated Surgically. Douglas Robb 369
Subtotal Esophagectomy for Bleeding Esophageal Varices. Denton A. Cooley and Michael E. DeBakey 369
Mesothelial Cysts in the Posterior Mediastinum. Giovanni Rollo 370

Miscellaneous

Therapy of Myasthenia Gravis; Indications and Limitations of Thymectomy. G. Bocchetti and A. Lucifero 370
The Risk of Anesthesia in Thoracic Surgery. Henri Le Brigand, Odette Lefebvre de Herrera, and Jacqueline Lequesne-Delfontaine 408

SURGERY OF THE ABDOMEN

Gastrointestinal Tract

Experiences with Upper Gastrectomy, Its Relationship to Esophagitis, with Special Reference to the Esophagogastric Junction and Diaphragm; a Study in the Dog. Elvin W. Hoag, Lawrence B. Kiriluk, and K. Alvin Merendino 372
Total Gastrectomy with Replacement Utilizing the Transverse Colon; Preliminary Report. David H. Watkins, George Wittenstein, and Jack Daniel 372
Combined Abdominoperineal Herniorrhaphy for Massive Rectal Prolapse. Edward T. Newell, Jr. 373
Duodenal Ulcer in Children; 2 Cases of Ulcer with Stenosis. Marcel Morin, Alain Mouchet, and Marthe Gautier 373
Colonic Resection for Diverticulitis. Edward Wilson 373
Carcinoma of the Colon with Special Reference to Prevention of Recurrence. Warren H. Cole, Douglas Packard, and Harry W. Southwick 373
Cancer of the Large Bowel; a Follow-Up Study of 420 Cases from a Private, a Charity, and a Veterans Hospital. Duncan A. Cameron, Henry A. Chapnick, and Don W. McLean .. 374
Significance of Reduction of the Intestinal Flora Prior to Operations on the Colon or Rectum. C. V. Munthe Fog 374
The Blood Groups in Relation to Peptic Ulceration and Carcinoma of Colon, Rectum, Breast, and Bronchus; an Association Between the ABO Groups and Peptic Ulceration. Ian Aird, H. H. Bentall, J. A. Mehigan, and J. A. Fraser Roberts 411
The Causal Relationship Between Benign Epithelial Tumors and Adenocarcinoma of the Colon and Rectum. K. A. Hultborn 412

Liver, Gallbladder, Pancreas, and Spleen

An Unusual Complication of Needle Biopsy of the Liver; Report of a Case. Allan A. Kaplan, Alfred Frobese, and Henry L. Bockus 375
The Management of Obstructive Jaundice in Infancy. E. M. Greaney, W. H. Snyder, Jr., and Lawrence Chaffin 375

Experiments on Oxygen Saturation and Pressure in the Portal Vein After Ligation of the Hepatic Artery. Emil Buecherl and Walter Dueben. 375
The Role of Intestinal Bacteria in Liver Necrosis Following Experimental Excision of the Hepatic Arterial Supply. William E. Schatten.... 376
Primary Carcinoma of the Liver. J. A. Coleman, R. D. Haines, and Charles Phillips..... 376
Postcholecystectomy Amputation Neuroma. Robert H. Hume and Robert W. Buxton..... 377
Ductal Changes in Chronic Pancreatitis. James J. Berens, Archie H. Baggenstoss, and Howard K. Gray..... 377
Carcinoma of the Head of the Pancreas; a Review of 49 Personal Cases. R. G. Moore and J. D. Younghusband..... 378
Results of Treatment of Carcinoma of the Pancreas. Edward S. Stafford, I. Ridgeway Trimble, and John N. Classen..... 378

Miscellaneous

Factors Involving Wound Dehiscence; a Study of 1,000 Cases. Robert L. Marsh, Joseph W. Coxe, III, and G. Arnold Stevens..... 378
Mesenteric Chylangioma; with Report of 2 Cases. James G. Kanski..... 379

GYNECOLOGY

Uterus

Surgery in Connection with Double Uterus; Hemihysterectomy and Parietal Hysterosympexy. R. Bourg and G. Lambert..... 380
Retention of Fragments of Fetal Bone in the Uterine Cervix for 10 Years. Marianne Basch. 380
Prophylaxis of Cervical Cancer; Its Diagnosis in Its Noninvasive State. P. Funck-Brentano... 380
Lymphoglandular Diffusion of Cancer of the Uterine Cervix. Pietro Marziale..... 380
Pelvic Eviscerations in Cancer of the Uterine Cervix; Technique and Indications. Comte and Bottou..... 381
The Vaginal Smear as a Prognostic Aid in Carcinoma of the Cervix Treated According to the Individualized Stockholm Method. Gertrude Kohn..... 410

Adnexal and Periuterine Conditions

Anatomoclinical and Histogenetic Considerations with Reference to the Tumor of Brenner; Apropos to a Personal Observation. Enrico Ferrario..... 381
Removal of a 184 Pound Ovarian Tumor, and Observations Regarding Splanchnic Shock. Dan. H. Eames, Jr..... 382
Ovarian Carcinoma; Risk of Preserving the Ovary. Clyde L. Randall..... 382

Miscellaneous

Tuberculosis of the Female Genitalia and Sterility; Considerations Based on a Series of 230 Treated Patients, of Whom 100 Were Operated Upon. C. Fernandez-Ruiz..... 382
Pelvic Pain Based on a Vascular and Autonomic Nervous System Disorder. Howard C. Taylor, Jr..... 383

OBSTETRICS

Pregnancy and Its Complications

Clinicostatistical Study on the Incidence of Obstetrical Complications, with Particular Regard to Seasonal Influences During the 12 Year Period of 1941–1952 at the Obstetrical and Gynecological Clinic of the University of Padua, Italy. G. Franco and A. Onnis..... 384
Malignant Hypertension Supervening Rapidly on Pre-Eclampsia. T. B. Counihan and It Doniach..... 384
Indications for and the Scope of Indirect Placentography in the Diagnosis of Placenta Previa. U. Borell, I. Fernström, and A. Westman.. 384
An Instance of Intraepithelial Epithelioma of the Uterine Cervix Disclosed in the Course of Pregnancy; Electrocoagulation; Normal Epithelization. P. Isidor, R. Chasques, and J. Fradin.. 384
An Instance of Postabortive Perfringens Septicemia with Anuria, Treated by Exsanguinotransfusion and Typhomycine; Recovery. J. Lapeyrere and J. Ducos..... 385
Acute Tuberculous Hepatitis in a Pregnant Woman. Tevfik Remzi Kazancigil, Cezmi Kazancigil, and Mes'ut Vahdat..... 385
ABO Blood Groups and Toxemia of Pregnancy. L. A. Pike and A. M. Dickius..... 411

Newborn

In Regard to 152 Births of Malformed Infants; Their Relative Frequency in Certain Periods of the Year. J. Ravina, J. J. Daunay, and P. Benamour..... 386

Miscellaneous

High Oxygen and Hyalinelike Membranes. Paul D. Bruns and Lloyd V. Shields..... 386
Adrenal Virilism in the Female Child and Adult. E. Stewart Taylor and Robert H. Snow.. 386

GENITOURINARY SURGERY

Adrenal, Kidney, and Ureter

Acute Tuberculous Hepatitis in a Pregnant Woman. Tevfik Remzi Kazancigil, Cezmi Kazancigil, and Mes'ut Vahdat..... 385
Penetrating and Perforating Wounds of the Trunk with Renal Involvement; Observations on Manner of Wounding, Character and Path of Missile, and Associated Injuries. Frederick A. Lloyd..... 387
Puncture Biopsy of the Kidney. F. Reubi..... 387
New Procedures for the Functional Exploration of the Kidney. J. Traeger..... 387
The Classical and the Modern Tests of Renal Function in Urologic Practice and Research. J. Minder..... 388
Neoplasms of the Ureter. J. H. J. Van Der Vuurst de Vries..... 388

A Contribution to the Clinical Picture of Ureteral Tumors with Particular Reference to the Benign Primary Tumors. T. Burckhart, E. Schmidt, and W. Busanny-Caspari 389
The Roentgen Diagnosis of Polycystic Kidneys. Lars Billing 409

Bladder, Urethra, and Penis

Radical Cystectomy for Advanced Carcinoma of the Bladder. Emile Sayegh 389
Reconstruction of the Anterior Urethra in Hypospadias by the Buried Skin Strip Method; a Simplified and Improved Technique. J. C. Mustardé 389

Genital Organs

Experience with "ST 52-ASTA" in the Treatment of Prostatic Cancer. R. Carow 390

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, etc.

Conditions of the Bones, Joints, Muscles, Tendons, Etc.

Observations on the Course of Skeletal Tuberculosis Under the Influence of Antibiotics. K. Daubenspeck and E. Rausch 391
Tuberculous Cystic Osteitis. L. Pellegrini 391
The Chemotherapy of Orthopedic Tuberculosis. F. Harwood Stevenson 391
Chemotherapy of Tuberculosis of Bones and Joints. M. C. Wilkinson 392
The Natural History of Osteoid Osteoma; with a Report of 20 Cases. J. S. R. Golding 392
A Peculiar Joint Disease; Systemic Calcification of Articular Cartilage. R. Marziani 392
Hydrocortisone in Tennis Elbow. D. E. Freeland and M. de G. Gribble 393
Tennis Elbow (Epicondylalgia Externa): Treatment with Hydrocortisone. C. E. Quin and F. A. Binks 393
Tennis Elbow; Treated with Hydrocortisone Acetate. A. H. G. Murley 393
Idiopathic Scoliosis; the Prognosis, Diagnosis, and Operative Indications Related to Curve Patterns and the Age at Onset. J. I. P. James 393
Osteomyelitic Foci of the Neck of the Femur. L. Bitossi Coronedi 393
Popliteal Cysts. J. L. Oggioni 395
Calcification of the Intervertebral Discs in Childhood. Frederic N. Silverman 409

Surgery of the Bones, Joints, Muscles, Tendons, Etc.

The Traumatic Anatomy and Treatment of Acute Acromioclavicular Dislocation. J. S. Horn 395
Selection of Skin Incisions in Surgery of the Hand. F. Fusi 396
Articular Transplants from Foot to Hand. E. Marcer 397
Finger Flaps. O. W. Wickstrom and B. E. Bromberg 397
Treatment of Meniscal Rupture of the Knee Joint; a Follow-Up Examination of Material in Which Only the Ruptured Part of the Meniscus Had Been Removed. Torleiv Aarstrand 398
The Compression Method of Key-Charnley in Resection of Knee for Tuberculosis. D. R. Zurovac and G. Senis 398

Fractures and Dislocations

Isolated Fracture of the Small Tuberosity of the Humerus. Antonio Mignogna and Eugenio Jannelli 399
The Use of the Acrylic Head Prosthesis in High Fractures of the Femoral Neck. J. C. F. Cregan 399
Treatment of Fractures of the Tibial Condyles by Active Movement Therapy. R. V. Lindholm 400
A New Method of Treatment for Fractures of the Calcaneus. F. A. Mandruzzato and G. Brunelli 400

Orthopedics in General

Development of Progressive Changes in Muscles Paralyzed by Peripheral Nerve Injury. C. Poglayen 401

SURGERY OF BLOOD AND LYMPH SYSTEMS

Blood Vessels

Transplantation of the Saphenous Vein for Postphlebitic Stasis. Richard Warren and Theodore R. Thayer 403
Surgical Management of Ulcerative Stasis Disease of the Lower Extremities. Ormand C. Julian, William S. Dye, and John Schneewind 403
Surgical Reconstruction of the Superior Vena Cava. J. Gordon Scannell and Robert S. Shaw 403

Blood; Transfusion

Determination of the Survival of Transfused Red Cells by a Method of Differential Hemolysis. Thomas H. Hurley, Russell Weisman, Jr., and Angela E. Pasquariello 404

Lymph Glands and Lymphatic Vessels

Lymphogranulomatosis Benigna; A Clinical and Histopathological Study of Its Relation to Tuberculosis. Lennart Zettergren 404

SURGICAL TECHNIQUE

Operative Surgery and Technique; Postoperative Treatment

The Role of Hibernation and of Decapsulation in the Treatment of Postoperative Anuria. E. Laduron and de Ville de Goyet 405

Antiseptic Surgery; Treatment of Wounds and Infections

Penetrating and Perforating Wounds of the Trunk with Renal Involvement; Observations on Manner of Wounding, Character and Path of Missile, and Associated Injuries. Frederick A. Lloyd 387

Infections Occurring During Chemotherapy; a Study of Their Frequency, Type, and Predisposing Factors. LOUIS WEINSTEIN, MARTIN GOLDFIELD, and TE-WEN CHANG..... 405
Experimental Allergic Encephalitis in Animals, and Its Bearing Upon the Etiology of Neuroparalytic Accidents Following Antirabies Treatment in Man. GEORGE A. JERVIS..... 405
The Treatment of Tetanus; Role of the Anesthetist. PATRICK SHACKELTON..... 406
Antiserum in the Prophylaxis of Rabies. KARL HABEL..... 406
Clinical Evaluation of Topical Antibiotic Therapy. ALFRED J. SURACI..... 407

Anesthesia

The Overuse of Carbon Dioxide Absorption in General Anesthesia. W. N. KEMP..... 407
Automatic Electroencephalographic Control of Thiopental Anesthesia. DONALD K. KIERSEY, ALBERT FAULCONER, JR., and REGINALD G. BICKFORD..... 408
The Risk of Anesthesia in Thoracic Surgery. HENRI LE BRIGAND, ODETTE LEFEBVRE DE HERRERA, and JACQUELINE LEQUESNE-DELFONTAINE..... 408

PHYSICOCHEMICAL METHODS IN SURGERY

Roentgenology

Cerebral Angiography in the Diagnosis of Intracranial Lesions. OSCAR SUGAR..... 357
Indications for and the Scope of Indirect Placentography in the Diagnosis of Placenta Previa. U. BORELL, I. FERNSTRÖM, and A. WESTMAN.. 384
Some Factors which Affect the Value of Carotid Angiography in the Diagnosis of Brain Tumor. ERNEST H. WOOD..... 409
The Study of Mitral Regurgitation by Roentgen Kymography, with Observations on the Movement of Cardiac Calcifications. VICTOR A. MCKUSICK..... 409
The Roentgen Diagnosis of Polycystic Kidneys. LARS BILLING..... 409
Calcification of the Intervertebral Discs in Childhood. FREDERIC N. SILVERMAN..... 409
The Value of Radiation Therapy in the Management of Intrinsic Tumors of the Spinal Cord. ERNEST H. WOOD, ALFRED S. BERNE, and JUAN M. TAVERAS..... 410

Miscellaneous

The Vaginal Smear as a Prognostic Aid in Carcinoma of the Cervix Treated According to the Individualized Stockholm Method. GERTRUDE KOHN..... 410

MISCELLANEOUS

Clinical Entities—General Physiological Conditions

ABO Blood Groups and Toxemia of Pregnancy. L. A. PIKE and A. M. DICKIUS..... 411
The Pathogenic Etiology of Occupational Tumors. G. DI MACCO..... 411
Malignant Transformation of Squamous Epithelium; a Cytochemical Study with Special Reference to Cytoplasmic Nucleic Acids and Proteins. GUNNAR MOBERGER..... 411
Blood Groups in Carcinoma of the Lung. R. B. MCCONNELL, C. A. CLARKE, and F. DOWNTON. 411
The Blood Groups in Relation to Peptic Ulceration and Carcinoma of Colon, Rectum, Breast, and Bronchus; an Association Between the ABO Groups and Peptic Ulceration. IAN AIRD, H. H. BENTALL, J. A. MEHIGAN, and J. A. FRASER ROBERTS..... 411
The Causal Relationship Between Benign Epithelial Tumors and Adenocarcinoma of the Colon and Rectum. K. A. HULTBORN..... 412
Development of Sarcoma After Trauma. GEORG EBERT..... 412
Tolerance of Adult Rats to Profound Hypothermia and Simultaneous Cardiac Standstill. SUAD A. NIAZI and F. JOHN LEWIS..... 412

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Collective Review

A HALF CENTURY OF EFFORT TO CONTROL CANCER

An Appraisal of the Problem and an Estimation of Accomplishments

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The twentieth century opens as the experimental era with the systematic study of tumors throughout the animal kingdom, and it seems likely to be noteworthy as a period of specific etiological investigation which promises to separate many neoplastic diseases formerly held to be closely related. It may thereby prove to be the era of successful therapeutics and prophylaxis.—JAMES EWING (1919)

THIS QUOTATION from Ewing's treatise on neoplastic diseases indicates the foresight he had of the accomplishments and goals in the attack upon cancer during the Twentieth Century.

At the completion of the first half of the twentieth century, the methods of controlling and curing cancer represent one of the major activities of peacetime effort. Millions of dollars are spent yearly by voluntary and governmental agencies. Countless investigators in every field of the biological and related sciences are investigating the cause and nature of cancer. Thousands of articles and numerous books devoted to the cancer problem are being published. Special societies have been formed to disseminate knowledge of cancer both to the laity and the medical profession. Specialized hospitals and divisions within general hospitals have been developed for the diagnosis and treatment of cancer. The development of systems of nomenclature, tumor registries, and biometrics applicable to cancer has gained momentum. Noteworthy discoveries in chemistry, physics, physiology, biology, and surgery have led to great improvements in radiation therapy, chemotherapy, hormone therapy, and the surgical sciences available to the cancer patient.

Despite these tremendous gains developed during the first 55 years of the twentieth century, the number of people who develop cancer and those who die from it continues to increase at alarming rates. The paradox of increased incidence and death from cancer occurring simultaneously with unparalleled knowledge about this disease and the application of this information to the cancer problem in human beings invites critical analysis. Many brilliant scientists have contributed to these gains and deserve great gratitude and credit, but much remains to be accomplished in cancer therapeutics. This historical review will apotheosize

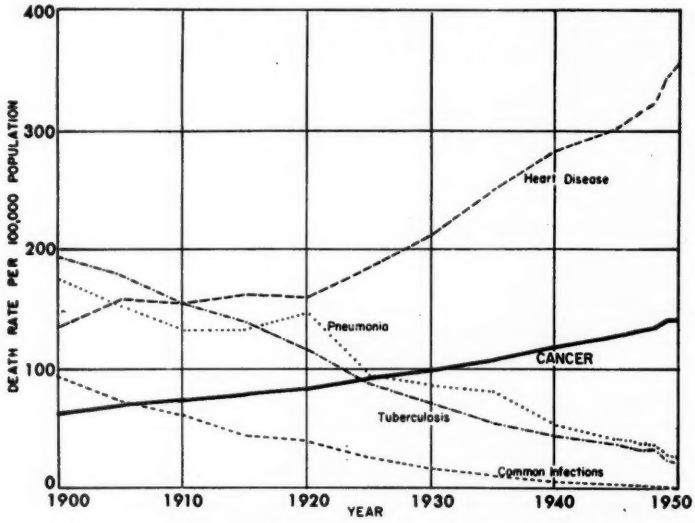


FIG. 1. Death rates of selected diseases, United States, 1900–1950. National Office of Vital Statistics. Statistical Research Section, American Cancer Society.

the past, humbly appraise the present, and hopefully look to the future.

"History," says Fuller, "maketh a young man to be old without either wrinkles or gray hair, privileging him with the experience of age, without the infirmities or inconveniences thereof."

THE MAGNITUDE OF THE CANCER PROBLEM AS INDICATED BY ITS CHANGING INCIDENCE— 1900 TO 1950

Prior to the twentieth century there was no compilation of mortality statistics in the United States. In 1900, the first year that mortality statistics were obtained, only 10 states and the District of Columbia were registered to supply these data. It was not until 1933, when Texas was finally admitted to the registration area, that the entire continental United States was represented. Interesting indices are uncovered by observing the mortality trends in the United States during the first half of the twentieth century. There was a rapid increase in the crude death rate from cancer since 1900. In 1950 there were 216,107 deaths due to tumors! Cancer, the second greatest cause of death, accounted for 150 deaths per 100,000 of population in the United States. In 1900, cancer was only the ninth most frequent cause of death in the United States, being responsible for 64 deaths per 100,000 of population, a total mortality of 48,000 citizens.

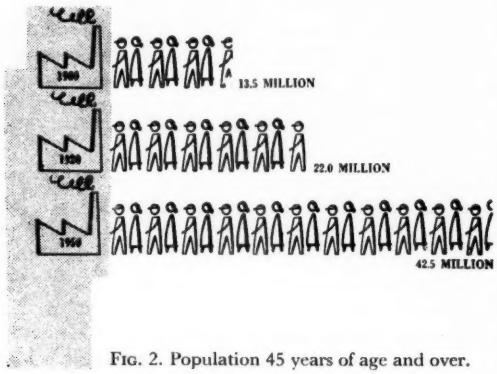


FIG. 2. Population 45 years of age and over.

This remarkable alteration in causes of death during the first half of the century is due to the successful control of infectious diseases by epidemiological, immunological, and antibiotic means. People live longer and thus eventually become more vulnerable to cancer occurrence. In 1900, of a total population of 76 million, there were only about 17.5 million over 40 years of age, or 23.3 per cent. The median age of the population was 22.9 years and the death rate from cancer, excluding leukemia and Hodgkin's disease, was 64 per 100,000. In 1950, the total population had increased to more than 150

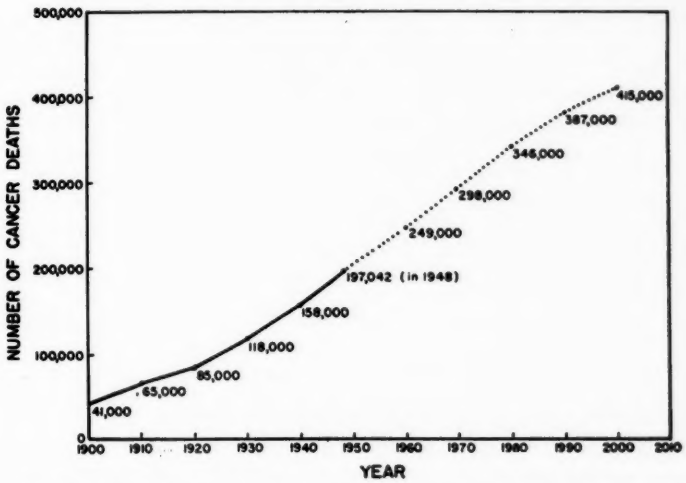


FIG. 3. Forecast of cancer deaths (if recent trends continue). Statistical Research Section, 3–50 American Cancer Society.

million and the percentage of people over 40 years of age numbered 53 million, or 35.2 per cent. The median age had increased to 30.2 years.

The present incidence of cancer permits rather alarming estimations. Under current conditions, 32 of every 100 children born are expected ultimately to develop cancer. Fifty million people, now healthy, will develop cancer during their remaining lifetime. It has been estimated, on the basis of the mortality rates in 1900, that 1 of 20 (5%) children born in that year would be expected to die of cancer. By 1940, the figure was 1 of every 8 (12%). It is estimated that in 1975 the number of people in our population over 40 years of age will be approximately 75 million and the citizens over 65 years of age will approach 22 million. At the end of the century, according to computations, the annual number of cancer deaths in the United States will be 415,000.

EVOLUTION OF BASIC RESEARCH IN THE ETIOLOGY AND NATURE OF CANCER

The therapeutic attack on a disease so protean in its manifestations as cancer requires the application of most scientific disciplines. Even such factors as sociologic trends have a direct bearing. At the turn of the century men interested in cancer research were considered charlatans or mystics for daring to penetrate into this mysterious phenomenon. Social apathy was reflected by absolute lack of governmental interest and intervention. Research of cancer at that time was performed in a hostile social environment. Contrast that situation with the present great public interest manifested not only by the generous voluntary contributions but also reflected by governmental support of numerous projects related to cancer control.

The unparalleled developments in physical sciences leading to the cataclysmic atomic bombs have contributed immeasurably to the cancer problem. The resurgence of endeavors in biophysical research directly benefits the cancer patient receiving radiotherapy as the improved knowledge of radiophysics permits improved techniques of irradiating cancer. The immediate application to the cancer problem of knowledge gained from this mammoth endeavor (the atomic bomb effort, designed for enemy destruction) reflects the present receptive state of mind which directs this information to the control of a biologic abnormality.

The cellular nature of cancer, accepted today with almost contumelious familiarity, was not developed until the great pathologists of the latter part of the nineteenth century—Müller, Virchow, Cohnheim, and others—established the morphologic nature of cancer. Virchow's statement "omnis cellula e cellula" established the fact that cancer consisted of cells which had

developed from other cells within the human organism.

Animal Oncology

The observation of Hanau in 1889 that cancer also occurred in animals and was capable of transmission did not arouse interest until Jensen, in 1903, demonstrated the spontaneous origin and transmissibility of tumors in mice. This discovery ushered in the era of animal experimentation. Breast and lung cancer are common in mice, rats, rabbits, and dogs. Leukemia occurs by predilection in fowl, herbiverous animals, and others. Melanoma develops in certain fish. The universality of cancer in the animal kingdom necessitated the development of pure strain animals as source material for studying the mechanism of tumor development, transmission, host reaction, and experimental therapy.

The Influence of Heredity on Animal Tumors

C. C. Little, after the turn of the century, started colonies of mice that were inbred over 20 to 30 generations, thereby developing a homozygous strain. The studies of Maud Slye (1879-1954) revealed the influence of heredity in spontaneous tumor formation in animals. Certain strains almost always develop lung tumors at 18 months of age (strain A mice), whereas others (C 57 black mice) will practically never have them. In addition, being host to a transplanted tumor is also based on certain inherited characteristics.

In 1936, Bittner made the extraordinary discovery that an extrachromosomal factor which was transmitted to the offspring by one suckling from its mother was responsible for the production of mouse breast cancer, and indicated how bizarre are the mechanisms of the epidemiology of carcinogens. The complexity of the genetics of tumor formation has been emphasized recently (1948) by Heston, who demonstrated that the genetic factors of certain tumors are multiple and are dependent upon at least four known genes.

Carcinogenesis

The observation by Percival Pott (1775) of scrotal cancers in chimney sweeps was the first suggestion of the possibility of carcinogenic agents. In 1915, Yamagiwa and Ichikawa produced cancer by the prolonged application of tar to the skin of animals. Fifteen years elapsed until Kennaway and his associates described purified carcinogenic compounds which were essentially polycyclic hydrocarbons. The first one described was 1,2,5,6-dibenzanthracene and later the active ingredient of tar was identified as 3,4-benzpyrene. The synthesis of the powerful carcinogen 20-methylcholanthrene, from bile acids, revealed a structural similarity between this carcinogen and steroids, and led to studies of the routes of intermediary metabolism of various body substances to discover if a metabolic rerouting of a substance internally led to the production of a carcinogen. The extensive investigations of Dobriner are classic; his identification of Δ^9-etiocholenolone in patients bearing cancer suggests a metabolic imbalance in these patients.

Numerous other carcinogens were identified, which produced both animal and human cancers. Certain azo dyes produce human bladder cancer. Roentgen-ray cancer afflicted early investigators in this field. Parasites were identified as producers of cancer. Fibiger was awarded the Nobel Prize in 1913 for his epidemiological studies of gastric cancer in wild rats, produced by a parasite with larvae which develop in the cockroach. The injection of Cysticercus crassicollis into rats produces liver cancer. Rous, in 1911, demonstrated the transmission of a filterable chicken sarcoma, and Shope, in 1933, discovered a virus capable of producing papillomas in a mammal (rabbit).

The observation that carcinogenesis can be induced in vitro by altering the physical properties of the cultural environment is of significant promise. Earle added methylcholanthrene to the culture of mouse fibroblasts, producing a cellular alteration reproducible after many hundreds of replantations. When remote descendants of this original culture were injected into mice, fibrosarcomas developed at the site of the injection.

The discovery of hundreds of chemically dissimilar agents capable of carcinogenesis and the bizarre and unpredictable reactions which occurred upon the application or ingestion of carcinogenic agents demonstrated that the metabolic status of the host played a significant role.

The Host Susceptibility to Tumor Formation or Acceptability of a Tumor Transplant

The role of hormones in tumorigenesis was first demonstrated by Loeb who, in 1919, showed

that ovarian hormones markedly influenced the growth of mouse tumors. In 1932, Lacassagne demonstrated the effect from purified estrogenic chemicals. The observation by Huggins (1941) of the effect of castration upon prostatic cancer in man ushered in the era of human cancer chemotherapy.

The studies of Sugiura, Kensler, and their associates pertaining to the production of liver cancer following the ingestion of butter yellow and the protection afforded by certain vitamins (riboflavin and others) focus attention upon the importance of diet and certain dietary supplements on the successful action of certain carcinogens.

The discoveries that certain purebred animals spontaneously develop cancer, the identification of viruses which are carcinogenic (Shope papilloma), the identification of the extrachromosomal mouse milk factor of Bittner and its bizarre epidemiology, the identification of numerous chemical and other carcinogens, and the effects of hormones and dietary supplements in enhancing or retarding the mechanism of these reactions indicate the complexities of carcinogenesis. Thus, the milk factor of Bittner is ineffective in producing mammary cancer unless a suitable substrate exists. If male mice were given estrogenic hormones in quantities to develop the breast to a structural and physiologic level, the milk factor would produce mammary cancer. This did not occur in male mice exposed to the milk factor but whose breasts were not developed by estrogens. A corollary in human cancer pathogeneis is the fact that some males treated by estrogens for prostatic cancer secondarily develop breast cancer.

Furth has reviewed the evidence that the development of certain cancers is the result of host alteration. Such tumors grow unrestrained in altered hosts but not in normal hosts. The theory of altered host effect was first postulated by Ribbert (1855–1920) who believed that malignant growths originate in loss of growth restraint by the adjacent tissue, which enables cells to proliferate and give rise to tumors. Examples of normal tissue restraint are evidenced by the cells of the epidermis which are believed to be held in check by the subjacent cells. An unknown regulator maintains the leukocyte count at 7,000 per cubic millimeter. Oxygen tension maintains the red blood cell count at 5 million per cubic millimeter. Cells of endocrine glands are rigidly controlled by the endocrine systems and by the metabolites or secretions of their "target organs." Thus, the parathyroid cells are influenced by the level of the plasma calcium and phosphorus. An intriguing example of thyroid and pituitary interdependence in relation to tumor development in these organs has been demonstrated by Bielschowsky who, in 1944, first showed that goiterogenic agents would produce thyroid tumors. Interference with thyroid hormone production such as that caused by thiouracil, which does not injure the thyroid cells but blocks their ability to synthesize TH and thereby stimulates the pituitary to discharge an increased quantity of TSH, results in a tremendous thyroid hyperplasia and adenoma formation, the effect of the TSH. Such tumors can metastasize to the lungs and can be grafted on mice whose thyroids are similarly blocked by thiouracil, but not on normal mice. Autonomous pituitary tumors which excrete excessive TSH produce similar thyroid tumors in mice. If the thyroid is injured with large doses of I^{131} with an abolishment of TH production, it causes a sustained stimulation (or loss of restraint of the pituitary) resulting in multiple pituitary adenomas. Thyroid grafts or the administration of thyroid hormones prevent the formation of pituitary tumors.

Any of the myriad combinations of the aforementioned factors can produce cancer. Any cell (or group of cells) in the multicellular animal, under proper stimulation and environmental conditions, can theoretically develop cancer. Etiologically, cancer is a group of diseases rather than a single disease entity. Thus, mammalian cancer arises apparently from a normal cell, grows in a disorganized manner, elicits a marked vascular response from the host to assure an effective blood supply for its continued growth, seldom if ever elicits an ingrowth of nerves, is species-specific and frequently individual-specific, and will grow vigorously in an emaciated body.

Many unexplained paradoxes exist. Certain chemicals (methylcholanthrene) produce cancer wherever placed, while betanaphthylene produces only cancer of the bladder, however given. Some metabolic conditions will inhibit the growth of certain cancers and enhance the growth of others. Urethane will produce temporary inhibition of growth of human myeloma and leukemia, but will markedly increase the incidence of pulmonary cancer within a certain strain of mice. Castrated newborn mice of a certain strain develop adrenal cancer in 100 per cent of the cases, as

shown by Little. Castration, on the other hand, may benefit some patients with prostatic cancer.

These observations would indicate, not only from an etiologic standpoint but also from the method of development, that most cancers have their own specific individuality. Thus, mammary cancer in mice, which has been most extensively investigated in this regard, depends upon at least four separate factors for its inception and growth: genetic, hormonal, carcinogenic (milk factor), and other environmental influences such as diet. Each plays its part, and a relative weakness of one factor can be offset by the increased strength of another, and substitution of certain factors may even be done. Thus, the milk factor may be substituted by a carcinogenic hydrocarbon, or the ovarian secretion may be supplanted by the adrenal hormones.

The formal genesis of cancer. The knowledge thus far achieved has answered many of the queries raised in Ewing's "causal genesis," but has left unanswered all of the questions raised in Ewing's "formal genesis," i. e., the specific alterations within the cells which cause that genesis in one part of a most beautifully organized system to rebel against the host and develop traitorously to the eventual destruction of the wondrous organization of which it was a functional part.

A voluminous literature has appeared within the last 2 decades aimed at identifying some of the mechanisms of the "formal genesis." The classic studies of Warburg, which demonstrated glycolysis under aerobic and anaerobic conditions of neoplastic tissue, show one of the greatest observed differences between normal and neoplastic tissues. An abnormal substance within neoplastic cells has not been identified; the differences are essentially of degree rather than of kind. Investigations into the nature of the enzyme systems made by Greenstein, and reviewed in his book (1947), have indicated quantitative alterations of certain enzymes. There tends to be a reduction in such enzymes as cytochrome and cytochrome oxidase. Some of the actions of the carcinogens are believed to be upon the genes, inducing chemical alterations of the nucleoproteins and presumably inducing mutations. Spencer (1945) has reported mutations in vitro with x-rays, and Demerec produced mutations in Drosophilia with a number of chemicals. Shimkin has called attention to the correlation between the "carcinogenicity in mice and mutagenicity in flies." Studies in this field continue unabated, and the intensity of the effort, no doubt, will be rewarded during the second half of this century by the identification of fundamental differences and the mechanisms by which these differences are developed by the cancer cell.

Application of Animal Cancer Research to Human Therapy

Although most of the information resulting from animal cancer research is not directly transferable for the understanding of human cancer, certain generalizations are permitted.

1. Cancer in the human being is not a single disease; it represents a cellular end result evoked by many different forms of stimuli, developed by the interplay of numerous metabolic reactions (some encouraging, others inhibiting the reaction), and, eventually, manifesting itself in different organs with an inherent impetus for growth and dissemination. The first step in untangling this complex problem is the identification and classification of the various cancers. Accordingly, the use of the all-embracing term "cancer cure" should be dropped and emphasis should be directed to specific neoplasms.

2. Heredity, which plays a major role in certain animal cancer experimentation, plays but a minor role in human cancer. There are no purebred human beings. Certain human neoplasms, such as retinoblastoma, xeroderma pigmentosa, and multiple polyposis of the colon, are inherited from parent to offspring according to genetic laws.

3. Certain species or strains of animals will react to cancer with varied reactions. Further understanding of this phenomenon may explain why certain cancers in human beings elicit a marked desmoplastic reaction aimed presumably at confining the cancer (scirrhous cancer), while others will react with the production of a medium which encourages cancer growth (inflammatory breast carcinoma).

4. In the past cancer was believed to be purely an autonomous growth which would grow wildly and of its own momentum, unhampered by the various control mechanisms of the body. This has been shown to be untrue in certain instances. The vivid evidence from cancer research has indicated that certain neoplasms, especiallyof theprostate and breast, are under hormonal controls. It has been demonstrated that hormones either influence the tumor directly or affect the substrate. These tumors do not grow autonomously and

according to their own governing laws, but rather represent abnormal deviants of growth which can be controlled in some instances by altering the host's chemical or hormonal status. This philosophy opens vistas for the understanding and control of cancer heretofore not possible when all cancers were regarded as growths with complete autonomy.

TUMOR PATHOLOGY

At the turn of the century, tumors were classified and catalogued according to their histologic appearance. The pathologists of the late nineteenth century had developed this science to a high degree. There was little comment about tumor etiology and histogenesis. Even though Virchow postulated his belief that cells arise from cells, many still believed in the fluid origin of cancer.

Pre-Twentieth Century Period.

The descriptions of tumors contained in the Ebers papyrus (1500 B.C.) were the result of the earliest study of the pathology of cancer. Hippocrates (460–375 B.C.) described cancers of the skin, breast, stomach, and cervix. Leonides of Alexandria (c. 180 A.D.) described retraction of the nipple in breast cancer. Paulus of Aeginia (625–690) distinguished chronic metritis from uterine cancer. During the Renaissance (1500–1700 A.D.) the decline in Galen's authority and distrust of his theories regarding cancer had a demoralizing effect upon cancer therapeutics and led to the use of chemical escharotics and to many bizarre hypotheses regarding cancer.

The humoral concept of cancer, which had blocked progress in a proper understanding of the disease ever since the time of Hippocrates, was finally discarded by LeDran (1685–1770). He demonstrated that cancer was a local manifestation in its early stage, spreading via the lymphatics to regional nodes and through the circulation to various organs. Morgagni (1682–1772) used autopsy material to distinguish gumma, exostosis, and lipoma from cancer.

Although the role of irritants had long been recognized in producing or aggravating neoplasms, Pott's (1714–1788) description of chimney-sweeps' cancer of the scrotum focused attention upon a specific, common, external cause of cancer and stimulated other similar observations.

Marie-François-Xavier Bichat (1771–1802), a gross pathologist, reorganized pathology according to the tissues of which the various body structures are composed. Laennec (1781–1826) first described melanoma as a separate form of cancer and distinguished between pulmonary tuberculosis and lung cancer. Sir Astley Cooper (1768–1841) first presented a concise clarification of the anatomy of the breast, its lymphatics, and tumors. Recamier (1774–1852) demonstrated the process of local infiltration by cancer and was the first to describe vein invasion; he coined the word "metastasis" to describe secondary brain growths from primary breast cancer.

The era of the histologic study of cancer had its inception from the introduction of the achromatic microscope in 1824. Schwann, in 1838, established the doctrine of the cellular structure and Müller, in the same year, demonstrated that cancer is composed of cells. Virchow (1821–1902), a pupil of Müller and known as the father of modern pathology, in 1858 published his book *Cellular Pathology*, one of the most important books in the history of medicine, and established the concept of tumor histogenesis ("omnis cellula e cellula"). All writers of that period, including Virchow, believed in the fluid origin of cancer and that it arose as an organized exudate of blood with overnutrition and overgrowth. This theory dominated all thought but nosologic differentiations were being made. Hodgkins (1789–1866) first described the syndrome "lymphogranuloma malignum," which was later given his eponym by Wilks. Hannover (1814–1894), a Copenhagen pathologist and a pupil of Müller, described the histologic features of epitheliomas but erred in believing them not to be cancer. Paget (1814–1899) first described Paget's disease of the nipple and bone, and emphasized the benign nature of giant cell tumor of bone. In 1864, von Recklinghausen, a pupil of Virchow, made important studies of bone pathology and described neurofibromatosis, attributing its origin to the endoneurium and perineurium. During this same period, at the end of the last century, Wölfler classified thyroid tumors. Cohnheim presented his data regarding the origin of cancer from abnormal cell rests in 1877. Thiersch, in 1865, demonstrated the origin of epitheliomas from epithelial cells and described preneoplastic changes, the result of tissue imbalances. Waldeyer, in 1863, demonstrated the nature of secondary tumors, a result of permeation or emboli in the blood or lymph vessels. Von Hansemann originated the concept of anaplasia and founded the modern

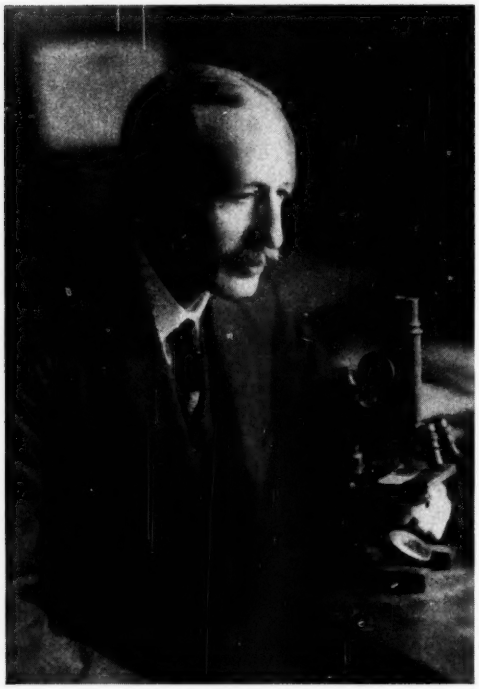


FIG. 4. James Ewing.

movement which attempts to grade tumors according to their degree of malignancy.

Twentieth Century.

The twentieth century thus opens with thorough descriptions of the morphology of tumors, e.g., the volume by Maximilian Borst in 1902. Max Otten, in 1906, first published cases of cancer in which the diagnosis was confirmed by autopsy. He correlated the clinical and pathologic findings, which was timely because attempts were being made to diagnose lung cancer by roentgenographic methods. In the same year, Maurice Chevassu presented a comprehensive thesis on testicular tumors.

James Ewing (1866–1943), the great American pathologist, devoted his lifetime to a study of the histogenesis of neoplasms. His approach can be best described by quoting from the preface of his classical book, *Neoplastic Diseases*, which was first published in 1919.

"Up to a very recent time it has been the prevailing impression that tumors fall into a limited number of

NEOPLASTIC DISEASES

A TEXT-BOOK ON TUMORS

By

JAMES EWING, A. M., M. D., Sc. D.
Professor of Pathology at Cornell University Medical College
New York City

WITH 479 ILLUSTRATIONS

PHILADELPHIA AND LONDON
W. B. SAUNDERS COMPANY
1919

FIG. 5. Title page of the first edition of Ewing's classic book, Neoplastic Diseases. (W. B. Saunders Company)

grand classes in which the forms occurring in the several organs are so nearly related as to be virtually identical. Hence the practical physician or surgeon has been content to regard all fibromas, sarcomas, or cancers as equivalent conditions without regard to the organ involved, and on this theory to treat the members of each class alike. Upon this theory also it was legitimate to conceive of a universal causative agent of malignant tumors and thus to subordinate many very obvious differences which clinical experience has established in the origin and behavior of different related tumors.

"I believe that this point of view has greatly retarded the progress of the knowledge of tumors, and it has been the writer's effort to combat such a conception, so far as present knowledge permits. He has thus endeavored to analyze the numerous etiologic factors which meet in such diverse fashions in the inception of tumors, to emphasize the general dependence of clinical course upon histologic structure, to trace the histogenesis to the last degree, impressing its essential importance when known, and to enumerate and contrast the more striking clinical features which are often highly characteristic of different

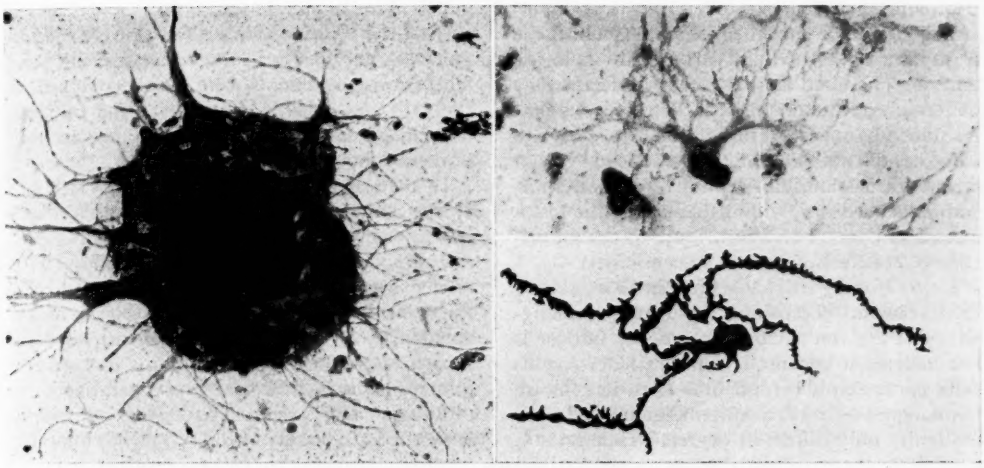


FIG. 6. Morphologic characteristics of certain tumor cells which are brought out by in vitro cultivation. a, left, Culture of sympathicoblastoma from 1.5 year old child. This shows central core of small cells surrounded by necrotic zone, through which epithelial tongues and beaded neurites extend some distance into the medium. b, (right top), Pericyte in culture of hemangiopericytoma (malignant glomus tumor). (bottom), Normal pericyte from heart capillary (Zimmermann). (American Journal of Pathology.)

tumors. . . The final classification of tumors must depend chiefly on histogenesis and structure."

Ewing commented on the four classifications—etiologic, regional, histologic, and histogenic—and asserted that it was only the last classification that allows a final breakdown of tumor types and permits a construction and understanding of the natural history of each specific tumor. The monumental work of Ewing presents the first great approach of "divide and conquer" for cancer. Current vital statistics do not present neoplasms according to their histogenic or histologic nosology, but rather on a regional basis. A recent (1954) publication of the nomenclature of tumors by the American Cancer Society, adopted by the World Health Organization, considers both regional and histogenic factors, and corresponds to the tumor nosology advocated by Ewing. In addition to Ewing's great work of classifying tumors, he further engaged in efforts to determine the radiosensitivity of neoplasms, a classical effort because it furnished important criteria for therapy, i.e., whether they should be treated by irradiation, surgery, or a combination of these methods.

Arthur Purdy Stout, of the Presbyterian Hospital, New York, a great contemporary pathologist, has aided oncology by his painstaking studies of subdividing tumor types and by describing their natural histories. Stout has contributed a classification of sarcomas which influences all therapy of these neoplasms.

Paul Klemperer, a student of Sternberg, has elucidated the histogenesis of lymphomas and Hodgkin's disease, has studied connective tissue diseases and elucidated the nature of the desmoplastic reaction induced by certain cancers.

The improvement of staining techniques by Weigert, Masson, and others has aided greatly in the understanding of neoplasms by affording morphologic diagnoses of tumor types. However, certain neoplasms do not permit classification in their natural habitat. Margaret Murray, working with Arthur Purdy Stout, cultivated human cancer in vitro and observed the cultural characteristics of tumors which tend to simulate their tissue of origin. The cultural studies of Murray were highly instrumental in identification of the hemangiopericytoma. These studies facilitate the diagnosis of a specific tumor in certain instances, not possible by routine microscopy. Thus, certain sympatheticoblastomas which defy diagnosis on in vivo histologic criteria can be identified on cultural analysis.

The development of new apparatus will broaden the horizon for the study of tumors. The innovations include the electron microscope, phase microscopy, and ultraviolet light phase microscopy. Newer tissue techniques, which include

tridimensional tissue culture, the growth of heterologous tumors in other animals (such as the transplant and growth of various tumors in the anterior chamber of the eye as performed by Greene), and the conquest of heterologous host resistance by making other animals receptive to transplanted human tumors as practiced by Toolan at the Memorial Hospital by the administration of cortisone, will further clarify the histogenesis of cancers and contribute to the knowledge of host resistance and susceptibility.

Degree of malignancy. Virchow, in 1858, can be credited with establishing the degree of malignancy of a given tumor. He stated, "Cancer is not malignant because it contains heterologous cells, nor cancroid benignant because its cells are homologous—they are both malignant and their malignity only differs in degree." Hansemann, from 1890 through 1900, elaborately described the phenomenon of anaplasia. He conceived of the degree of anaplasia as an expression of the degree of malignancy. The professional mind, however, was not geared for its acceptance at that time. In 1913, Salomon declared, "The prognosis of cancer of the breast is dependent in the first place upon the degree of malignancy."

Credit for determining the degree of malignancy on the basis of histologic criteria and the clinical application of this information are conceded to Broders, who, on March 6, 1920, published a description of the degree of differentiation and anaplasia. He classified the tumors into grades I to IV, grade I being the more differentiated and grade IV being the more anaplastic. Such a classification has proved its value in estimating the prognosis and even in determining the type of therapy.

Morphologic indices have certain limitations because the extent of the cancer at the time of its diagnosis is also important from a prognostic standpoint. Thus, Dukes has classified the stages of cancer of the rectum as A, B, and C, the stage depending upon the degree of extension, and Borrmann has formulated a similar staging for gastric cancer. Other criteria utilized by pathologists to grade the malignant quality of cancers are the extent of infiltration into the surrounding parenchyma, the presence or absence of encapsulation, the quantity and character of host reaction, and the evidence of metastases. These features, coupled with certain clinical indices (age, menstrual status, pregnancy), offer important signposts for prediction of the prognosis.

The histologic diagnosis of tumors (biopsy). At the turn of the century biopsies were rarely used to guide the surgeon in his operative dissection; in fact, strong arguments were weighed regarding the pros and cons of biopsy. Hellwig, in 1932, and Haagensen (1940) recited a detailed account of these controversies.

In 1878, Ruge, a gynecologist, and Veit, both of the University of Berlin, wrote that every operative procedure on the cervix should be preceded by the harmless procedure of biopsy. This advice was coincident with, and provoked by, the operation of abdominal hysterectomy as advocated by Freund, an operation attended by such a high mortality at that time that an absolute diagnosis had to be preoperatively established. The greatest opponents of biopsy were the pathologists of the day, who, unaccustomed to surgical pathology, were content to study autopsy material. Thus, Ruge, in 1890, pleaded with the current gynecologists to ignore the criticisms of pathologists and to perform their own histologic diagnoses. By 1900 the biopsy was frequently accepted. In 1895, Cullen, in the United States, devised frozen sections of cervical tissues and uterine curettings, and this became the procedure in Kelly's clinic. In 1905, the pathologist Louis B. Wilson described a modification of the frozen section, and the preoperative biopsy became a routine procedure at the Mayo Clinic. This was the greatest stimulus for the performance of biopsy in America. In 1915, Ewing advocated, although with many reservations, the extensive employment of biopsy; he urged great reliance on the gross examination of the whole tissue and strongly condemned the use of frozen sections. A committee of the American Society for the Control of Cancer studied this problem and its chairman, Bristol, suggested that state laboratories offer free diagnoses of tissues suspected of being cancerous. Bainbridge, at that time, wrote a number of articles indicating that biopsies had done harm. In 1917, the editor of the New York Medical Record wrote vehemently against the use of biopsies. Greenough, of the American College of Surgeons, sent questionnaires to the medical profession and the consensus of opinion as expressed by 134 of the physicians solicited was as follows: "Superficial and ulcerated lesions are the only ones in which fragments of tissue may be safely removed for microscopic diagnosis. In deep tumors, where the exploratory incision necessarily opens up normal

tissue to infection, exploratory excision of suspected tissue is to be condemned, and should be avoided. Where other sources of diagnosis have been exhausted, an exploratory excision with immediate frozen section diagnosis, and immediate performance of a radical operation if it proves necessary, is the least dangerous procedure for the patient."

Bloodgood, who worked in Halsted's clinic in 1914, stated that the mistake of diagnosing cancer as a benign lesion had occurred only twice. The mistake of treating a benign lesion as malignant, although mutilating, was considered to have no element of danger. Among 542 benign lesions, 54 (10%) had been incorrectly treated for cancer. Bloodgood promulgated the rule that when in doubt, the breast lesion should be treated as a cancer. In a series of 469 connective tissue tumors, 83 had been incorrectly diagnosed on the basis of clinical evidence and the patients were subjected to radical surgical extirpation; in 5 an unnecessary amputation was performed. The 10 per cent error by such masters of clinical diagnoses as Halsted and Bloodgood would suggest a much higher error by most surgeons of the era.

The formal biopsy has become a routine procedure today. In 1930, Martin and Ellis reintroduced the biopsy by needle puncture and aspirations, which procedures are still routinely used by many surgeons. Since then, various instruments have been designed either for aspiration or punch biopsies, and these procedures, although controversial, have become commonly employed.

Papanicolaou has recently developed and popularized the examination of exfoliated cells for cytodiagnosis of cancer. This method of microscopic diagnosis is particularly useful as a screening technique for detecting cancers of the cervix and bronchus. Its use has extended to the diagnosis of cancers of the prostate, rectum, paranasal sinuses, stomach, and colon. Various instruments containing rough edges such as the gelfoam sponge of Gladstone and the Ayre stomach brush are utilized to obtain smears of tumor cells from various sites.

IMPROVEMENT IN CANCER DIAGNOSIS

Cancer, to be cured, depends upon a chain reaction of events, each mutually dependent upon the others: (1) the patient must present himself to a physician, identifying certain symptoms or signs which might be caused by cancer; (2) the doctor must maintain a high degree of suspicion of cancer for every patient whom he examines, especially in the older age brackets; (3) a diagnosis must be established by histologic criteria; and (4) early and adequate therapy must be instituted. In tracing the improvement in cancer diagnosis, one must envision the situation as it existed at the turn of the century. Cancer was the ninth most frequent cause of death in 1900; hence it is not surprising that efforts to control infectious diseases dominated medical thought. There was practically no cancer research; the occasional individual who manifested an interest in this disease was regarded with suspicion. Many hospitals refused admission to patients with cancer, considering the disease hopeless. There was only one cancer hospital, no cancer clinics, and no detection centers. No education for the public existed and the only exposure the physician had to the disease was in the morgue or the pathology laboratory, or as the occasional assistant of a bold surgeon. Vital statistics were nonexistent. X-rays had been discovered only 5 years before and radium but 2 years previously. Surgery was crude, anesthesia was inflexible, blood grouping had not been discovered, and surgical physiology was in its infancy. The first successful stomach operation had been performed but 19 years previously and the radical hysterectomy was being developed. Neoplasms arising in the lung, esophagus, pancreas, liver, and central nervous system were not considered in the surgical domain. There were no cancer societies, there was no federal legislation, and the only state aid was an appropriation of ten thousand dollars by the New York State legislature in 1898 for a program of cancer research lasting 2 years.

The developments from that period to the present one can best be followed by describing them under the specific fields of endeavor. The enlightenment of the public regarding tumor identification at the lay level and the educational program of the profession represent a harmonious synchronization of efforts of various organizations aimed at curbing human cancer. The organization of special cancer societies and cancer divisions within other professional societies reflects the unrest which exists within the minds of both the lay and professional personnel regarding the inadequacy of methods to control cancer. Many of the present developments of education both of the laity and of the profes-

FIG. 7. Cancer clinics approved by the American College of Surgeons, 1953. Each dot represents an approved cancer clinic or cancer diagnostic clinic (American Cancer Society).

sion, the availability of funds for research, and the development and support of journals to disseminate cancer knowledge are the results of the activities of cancer organizations. The constructive cancer propaganda of the American Cancer Society has acquainted a huge proportion of the population with the nature and danger signs which might be cancer. The activities of the Cancer Division of the American College of Surgeons have penetrated into every walk of medical practice. Since 1937, with the inauguration of the National Institute of Cancer, great achievements by the government in this field have taken place.

THE AMERICAN CANCER SOCIETY

This Society was founded in New York in May, 1913, and was originally called the American Society for the Control of Cancer. During the first year, the society raised $10,000 by popular subscription and that year published the first article in a lay journal, *The Ladies Home Journal*. In 1936 the society reorganized and in 1945 it "adopted the name 'The American Cancer Society'." The program was divided into three main categories: (1) medical and scientific, to include professional education, professional service, statistical research, and a medical library; (2) field relationships to include public education, volunteer service to the cancer patient, recruitment and training of volunteers, and fund raising; (3) the administration program. The society's total budget of $10,000 in 1933 increased to $19,750,000 in 1953 and 1954. A brief review of some of the accomplishments of this great voluntary organization will demonstrate the direction of the effort. A clinical fellowship program received $394,330 in 1952–1953, with the current program supporting 135 fellows and 4 trainees in 44 institutions. The oldest of the Cancer Society's sponsored publications, *Cancer*, has almost 5,000 paid subscribers. *A Bulletin of Cancer Progress* (Ca) has 56,000 subscribers. A series of *Cancer Monographs* are distributed to 190,900 physicians throughout the country. There are 539 approved cancer clinics, 113 diagnostic clinics, and 99 detection centers partly supported by the Society. The Cancer Society has a statistical research unit which has prepared and published a *Manual of Tumor Nomenclature and Coding*, which has been translated into six languages and is being utilized by the World Health Organization. The Society supports cancer research under advisement from the Committee on Growth of the National Research Council.

THE CANCER CLINIC APPROVAL PROGRAM OF THE AMERICAN COLLEGE OF SURGEONS.

To the Clinical Congress of the Surgeons of North America belongs the credit for initiating the cancer program in the United States. At its

FIG. 8. Cancer detection centers approved by the American College of Surgeons, August, 1953. Each dot represents an approved center. Statistical Research Section, American Cancer Society, 9–53.

November 1912 meeting, the Clinical Congress appointed a committee, with Thomas S. Cullen of Baltimore as Chairman, to wage a campaign of publicity in order to acquaint people with the fact that cancer is curable if detected at a sufficiently early stage.

From this November 1912 meeting of the Clinical Congress of the Surgeons of North America came the impetus for the founding of the American College of Surgeons. With the authority of the Clinical Congress an Illinois charter was obtained on November 25, 1912, and at a meeting in Washington on May 5, 1913, the American College of Surgeons officially came into being. Four years later (1917) the College took over the Clinical Congress and has made it a featured part of its yearly activities.

One strong impetus for the College's activities in its cancer program was given in 1921 when, at the instigation of Ernest A. Codman, the Registry of Bone Sarcoma was established. The nomenclature of bone tumors adopted in 1921 by Codman, Ewing, and Bloodgood has been little changed. More than 2,100 cases with complete follow-up analyses were reported up to 1938. Branch has asserted that there are approximately 956 approved hospitals which could accommodate a cancer service but do not have any.

In 1922 the Committee on the Treatment of Malignant Diseases by Surgery, Radium, and X-ray, under the Chairmanship of Robert B. Greenough, was established by the Board of Regents of the College; this committee established local committees of the College to investigate the care of cancer patients within hospitals in eleven American cities. Statistical studies of cancer of the cervix, breast, and mouth were done and conclusions were published during the next 5 years. With the approval and at the request of the directors of the American Society for the Control of Cancer, the American College of Surgeons in 1930 formulated a minimum standard for cancer clinics in general hospitals, and through correspondence and personal communications with interested parties in hospitals throughout Canada and the United States recommended the formation of cancer clinics. Existing facilities were surveyed by the College in 1931, and in 1933 the College published the first list of cancer clinics to which it was able to give its approval on the basis of compliance with the minimum standards. The list has grown until there are 698 approved cancer clinics in the United States, its territories, Canada and Cuba, as of September, 1954.

THE NATIONAL CANCER INSTITUTE

This Institute is one of the seven institutes which comprise the National Institute of Health, the research arm of the United States Public Health Service. The Institute and a National

Advisory Council were created in 1937 to combat the growing challenge of cancer. In the National Cancer Institute Act, the seventy-fifth Congress outlined the duties of the Institute and Council, gave them the broad powers necessary for a comprehensive attack on the cancer problem, and allotted funds for this purpose. The National Advisory Cancer Council serves as an advisory body to the Surgeon General of the Public Health Service.

The Institute's research staff is composed of approximately 400 scientists, technicians, and laboratory assistants who have from 100 to 150 research projects under way at all times. A new Clinical Center just completed is a combined 500 bed hospital and laboratory building which makes available the most modern facilities for research and patient care. The amounts allotted by the National Cancer Institute to the research grants program vary with its total appropriation from year to year, but since 1947 they have ranged from approximately $2,500,000 to $4,900,000 annually. The number of grants made since the Institute's establishment in 1937 exceeds 2,200 and totals over $22,000,000. Control projects supported by National Cancer Institute grants are directed at applying the results of laboratory and clinical research to the control of human cancer and the improvement of cancer services and facilities. The amounts allotted for these projects vary from $900,000 to $1,000,000 annually, and since 1946 $17,300,000 have been allotted for expansion of cancer control programs. During this time $14,815,000 have also been allotted in special grants-in-aid to institutions and individuals engaged in educational, research, and clinical projects dealing with cancer control.

Cancer Education.

Each accredited 4 year medical school participating in the program receives a grant not to exceed $25,000 annually; medical schools that give only the first 2 years of the medical course and dental schools receive grants not to exceed $5000. The amounts allotted annually for this teaching program have ranged from $1,500,000 to $2,225,000 per year. Over $8,000,000 in teaching grants have been given to 79 medical schools since July 1947, to augment the teaching staffs and to provide training material. Approximately 100 physicians for postgraduate cancer training are in training at any one time. Clinical traineeships totaling about $2,000,000 have thus far assisted 450 young physicians, including 14 women, in taking advanced training in radiology, surgery, pathology, and other specialties. More than 800 persons have been granted research fellowships up to the present time. The Institute currently has 161 active fellowships totaling $499,763.

FUNDS FOR CANCER RESEARCH

The immensity of the research projects is reflected by the amount of money being spent. In 1948, about $14,000,000 were spent for cancer research: $8,000,000 by the Federal Government, $3,000,000 by the American Cancer Society, and an estimated $3,000,000 by state governments, foundations, universities, and private philanthropies. In 1953, the countrywide budget for cancer research was about $15,000,000. Some of the money spent by the National Research Council for the Committee on Atomic Casualties is for cancer research. The amount spent by the Atomic Energy Commission directly for cancer research since 1949 amounts to about $323,000. About $1,000,000 were being spent to study radiation as it relates to cancer, and an additional $200,000 to supply certain radioactive isotopes to investigators in nongovernment institutions. In addition, cancer projects and facilities costing more than $4,000,000 are being established near atomic piles, and a training program and a grant-in-aid program costing more than $600,000 are in operation. The Government is spending more than $1,000,000,000 in research.

A few other cancer funds include the Damon Runyon Fund for Cancer started by Walter Winchell in the middle of 1937, which has collected over $2,000,000 to date. The Babe Ruth Cancer Fund has collected about $100,000. The Jane Coffin Child Memorial Fund for Cancer Research consists of a gift in trust of approximately $2,500,000. Insurance companies which paid out $241,000,000 for cancer deaths in 1947, allocated only $1,225,000 for medical research, almost entirely for cardiovascular diseases, but none for cancer research.

Expenditures for clinical prognosis, reporting systems, support and development of clinical facilities, ecology, and care of the hopelessly ill amounted to about $6,000,000 from the Federal Government, $9,000,000 from the American Cancer Society, and about $2,500,000 from

other sources for a total of $17,500,000. Thus the total expenditure equals about $31,500,000 per year for cancer. The 1953 appropriation by the Federal Government for cancer research and cancer control exceeds $19,000,000 and the American Cancer Society has raised over $19,750,000 for this purpose.

SOME ACCOMPLISHMENTS FROM THE CANCER CONTROL PROGRAM

Lay Education.

Lay education of the public is decried by some as harmful in spreading cancer phobia. Ewing once stated that no one has ever died from cancer phobia, although many die from cancer; therefore the continuing intelligent education of the public will bear fruit. More than 200 years ago, in 1734, the whole female population of the village of Besancon was overcome with fear of breast cancer. Vacher reported this incident following a surgeon's suggestion to the women of that city that they examine their own breasts. This was the first instance of mass education of the public regarding cancer identification and also the first instance of endemic cancer phobia.

Cancer Detection Services.

An attempt to identify the presence of cancer before it has given rise to clinical expression was begun in 1938 by 2 women physicians, Catherine MacFarlane of Philadelphia and Elise L'Esperance of New York. There are at present 240 detection centers throughout the United States. The doctor is being educated to perform cancer detection in his own office. On the basis of 52,000 examinations performed in more than 90 scattered centers, 8 cancers per 1,000 people examined have been discovered.

Improvement of Detection Techniques.

Whereas most cancers are visible by simple examination, the identification of others necessitates improvement in detection techniques. The development of the cytologic examination by Papanicolaou is a foremost improvement in this respect. Mass x-ray screening has been attempted, but it has not been found to be economical. The search continues for new methods of cancer detection techniques, such as analyses of blood serum and rapid methods of screening patients for gastric acidity by chemical methods. None are universally acceptable to date.

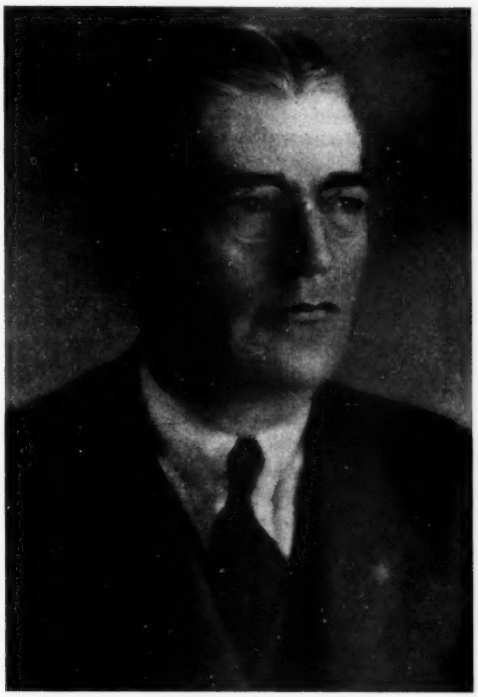


FIG. 9. Robert B. Greenough.

CANCER HOSPITALS

There are in the United States to date, 176 cancer diagnostic clinics, 539 cancer treatment clinics, and 11 hospitals devoted exclusively to cancer.

The first cancer hospital was opened in Rheims in 1740 under the direction of the Hotel Dieu as the result of the will of Jean Godinot, a Canon of the Rheims Cathedral. In 1779, because of the superstition that cancer was contagious, the hospital was moved outside of the city and named the Hospital St. Louis; it housed cancer patients until 1846, by which time the fear of contagion had subsided.

The first establishment of a cancer service in a general hospital occurred in England, at the Middlesex Hospital. John Howard, a pupil of Percival Pott, made the suggestion and in 1792 his plans were accepted and the first ward was started; it consisted of twelve beds for patients with cancer who might remain "until either relieved by art or released by death." In 1885 the ward occupied one whole floor; in 1900 it

consisted of a separate wing of 49 beds, and at present it represents one of the world's most famous cancer institutes.

In the United States the formation of the first cancer hospital can be attributed to J. Marion Sims. He first stressed the importance of a hospital devoted to gynecologic disorders, which resulted in 1855 in the formation of the Woman's Hospital. He constantly endeavored to treat cancer in that hospital but met rigid resistance both from his professional colleagues and the lay Board of Managers. Although he won international fame as a gynecologic surgeon, he was forced to resign from the Woman's Hospital on the basis of insubordination, and was ridiculed and threatened for his efforts to treat cancer. He urged that a separate pavilion be established for the treatment of patients with cancer; his plea resulted in an anonymous gift of $180,000 offered to the Woman's Hospital for that purpose. When this was refused, the sum was used as a nucleus for the creation of a cancer hospital —New York Cancer Hospital—whose cornerstone was laid May 17, 1884, and which in time became the present Memorial Center for Cancer and Allied Diseases. The reader is referred to a fascinating story of the visionary and controversial J. Marion Sims, in an article by Martin, Ehrlich, and Butler in *Cancer*, 1950, 3: 189.

The first government cancer hospital was the one organized by New York State in 1898—the Roswell Park Cancer Hospital in Buffalo, New York, now the largest in the United States.

At present there are 12 hospitals in the United States devoted exclusively to cancer:

City of Hope Medical Center.....California
Penrose Cancer Hospital.....Colorado
Pondville Hospital.....Massachusetts
Westfield State Sanatorium....Massachusetts
Ellis Fischel State Cancer Hospital..Missouri
Barnard Free Skin and Cancer Hospital
.....Missouri
John E. Jennings Hospital
.....Brooklyn, New York
Roswell Park Memorial Hospital
:.....Buffalo, New York
Francis Delafield Hospital.....New York
Memorial Center for Cancer and
Allied Diseases.....New York
M. D. Anderson Hospital for
Cancer Research.....Houston, Texas
Radiotherapy Institute and
Oncologic Hospital:.....Puerto Rico

The Recognition of Occupational Cancer.

It was natural to seek a cause for cancer in industry which was growing more expansive and complex with the exposure of workers to numerous elements, some of which were directly toxic and others apparently carcinogenic. The first such observation was made in 1775 by Percival Pott who described scrotal cancer in chimney sweeps. From 1873 to 1875, Volkman observed 3 patients with scrotal carcinoma which he believed was due to tar and paraffin distilled from soft coal. He also described a precancerous dermatitis in these workmen. In 1879, Harting and Hesse described cancer of the lung, called "miners' cancer," which had plagued the miners of the Erz Mountains for centuries. The authors believed the cancer was due to inhalation of mine dust—cobalt, nickel, bismuth, and arsenic. Even at the end of the nineteenth century, when radioactivity from the pitchblende of these mines was discovered, it was not considered of etiologic significance. Only recently (1932) has the lung cancer in these people been shown to be due to radioactivity.

In 1895, Rehn described papilloma and cancer of the bladder in men employed in the preparation of fuchsin. This was substantiated by the appearance of bladder cancer in numerous men employed in the dye industry. After the turn of the century, numerous industrial agents were found to cause cancer. In 1922 Southam and Wilson described mulespinners' cancer traced to the lubricating oil used by the mulespinners in the cotton mills in Manchester. Bridge and Henry were instrumental in making occupational cancer compulsorily notifiable in England and Wales. Young and Russell have used these data to report cancer mortality in various occupations (1926).

Hueper, of the United States Public Health Service, has been most active in tracing the relationship of certain industrial exposures to tumorigenesis. The following remarks are abstracted from his numerous publications. Some cancers of the urinary bladder are etiologically related to the aniline dye industry. Betanaphthylamine is the most potent and may be the only substance in the dye industry that produces bladder tumors. Its recognition has permitted control of this disease and has afforded compensation to those suffering from it. In 1942, certain cutane-

ous cancers were found to result from certain fractions of oils that had been cracked by a catalytic process in the petroleum industries. This substance, which has chemical properties resembling anthracene, is found to be carcinogenic only in mice, no cancers having occurred in men. Caution is being exercised in the petroleum industry. Cancer of the scrotum has been observed in petroleum workers who have been exposed to wax derivatives. There have been about 19,000 skin cancers in Great Britain in certain industries in which there was exposure to processed shale oil. Skin cancers occur in briquette workers; a total of about 18,000 skin cancers from tar or pitch has been reported from various countries. Cancer from arsenic is well known and represents an industrial hazard in sheep-dip workers, who are said to have developed cancer of the skin and lungs as a result of their contact with arsenic dust. Widespread use of arsenic in insecticides is a danger. Radiation carcinoma is well known, and radiation presents a definite hazard. Total body radiation from atomic bombs has resulted in an increased incidence of leukemia and represents an industrial hazard to those working in atomic piles and possibly those associated with atomic energy for peaceful purposes in the future. The work of Machle and Gregorius has demonstrated that chromate is a carcinogen, producing pulmonary cancer. Asbestos is similarly suspect, but its culpability has not been proved. In liquor refineries using the Mond process, there is a high incidence of cancer in the paranasal sinuses and the lungs. It is believed to be due to the inhalation of vapors of nickel carbonyl. The relationship of smoking to lung cancer awaits further proof. The observations by Martland of osteogenic sarcoma in girls who ingested small quantities of radioactive elements in luminous paint indicate this as a source of a powerful carcinogen. Studies relating to the industrial potential of liberating carcinogens and the cancers thereby formed have been a strong impetus for the control of these factors and the prevention of the production of carcinogens or for providing safety for the workers thereto exposed. A great debt of gratitude by society is owed to Hueper for his tireless efforts in this regard. The making of cancer a compensable disease indicates another step in the recognition of society's debt to the patient who develops cancer as a result of exposure during his work.

Methods for Reporting the End Results of Cancer Therapy

Richard von Volkmann was probably the first worker to present follow-up statistics when in 1875 he published the end results following the surgical treatment of breast cancer. The reporting of end results following efforts to cure cancer was first attempted by Alexander von Winiwarter, who was Billroth's assistant and who, in 1878, published a statistical evaluation of patients who had been operated upon in Billroth's clinic and had been followed for a given period (usually for 3 years). He showed that 4.7 per cent of 170 patients operated on for breast cancer were alive and well 3 or more years later. This observation had a profound effect upon the laity and profession alike, who believed that cancer was incurable.

From this humble beginning at the end of the nineteenth century, ever-expanding programs in cancer biometrics have materialized in the twentieth century. The establishment of vital statistics and the reportability of deaths in the United States since the turn of the century have made data available for computing the incidence and death rates of cancer. The compulsory reportability of cancer in England and Wales during the second decade of the nineteenth century has afforded that country some of the best data regarding cancer incidence in the world. In 1929 the League of Nations Health Organization, Cancer Commission, established a committee composed of J. Heyman (Radiumhemmet), A. Lacassagne (Radium Institute, Paris), and F. Voltz (Munich) who drew up rules for reporting end results of cancer treatment. One of the finest systems for observing patients and checking end results exists at Radiumhemmet, Sweden, where government subsidy has permitted a follow-up of almost every patient treated at that Institution since its founding in 1910.

Despite the tremendous interest in this problem, the development of complex statistical machinery for computing end results and their significance, and the employment of biometricians and statisticians by hospitals, and state and federal government agencies, there is still no universal method for reporting end results. In 1953, a joint committee was established in the United States to recommend rules aimed at eliminating the major causes of confusion. The

Committee was composed of representatives of the American College of Surgeons, the College of American Pathologists, the American College of Radiology, and the American Cancer Society, with the addition of one member-at-large from the National Cancer Institute. The Committee made the following criticisms of methods for reporting end results in present vogue and called attention to the widely different cure rates which are published for what appears to be the same type of cancer and the impossibility to tell if the differences are due to variations in the method of reporting the results. The principal reasons for this confusion seem to be:

Selection of cases. The result of therapy depends in no small measure upon the condition of the patient at the time treatment is initiated, and there are great variations in the type of patients coming to the attention of the various doctors. Some workers present only "hopeful" cases, some present all patients treated (whether hopeful or not), and some present all patients seen (including those not treated).

Proof of diagnosis. Some workers include only those cancers with microscopic confirmation of the diagnosis, and still others make no mention of the method of diagnosis.

Inadequate follow-up. Comparatively few doctors or hospitals are able to obtain a 5 year follow-up on every patient with cancer. Survival rates are usually based on those patients who were not lost to follow-up.

Cure rates versus survival rates. "Five year cancer cures" are distinguished from the "5 year cancer survivors" by the fact that the former are patients who are alive and apparently free of cancer 5 years after diagnosis, whereas the latter are patients who are alive but with evidence of cancer. Although both 5 year cure rate and 5 year survival rate are useful (though for somewhat different purposes), serious error results from mislabeling or failure to specify clearly which of the two is meant. Another difficulty which arises in this matter is the fact that in reporting the 5 year cure rate there has been no uniform method of recording patients who had cancer but died of causes other than cancer before the end of the 5 year period.

The rules for reporting 5 year end results of persons with malignant neoplastic diseases as recommended by the Joint Committee are:

1. Include all patients diagnosed as having a malignant neoplasm, whether treated or not. Whenever possible, all cancers should be classified according to the site of origin.

2. The cases reported should be divided as defined below:

Section A—Cases in which the patient has not been treated previously. The duration of these cases is measured from the date of the original diagnosis of the cancer.

Section B—Cases in which the patient has been treated previously. The duration of these cases is measured from the beginning of subsequent treatment.

The total number of patients in Sections A and B should always be reported. However, if the investigator so desires, he may report the full details for one of these two sections only. It is generally desirable to report every case from the date of the original diagnosis until the end of the 5 year period. If this is done, then all cases will fall in Section A. The detailed tabulation of Section B cases is designed primarily for the convenience of those investigators who wish to report on the efficacy of treatment for recurrent cancers.

3. Include only patients with an elapsed duration of at least 5 years. Report the status of each patient on the fifth anniversary. Each patient should be examined at least yearly.

4. The condition of patients classed as alive and free from cancer must be established through examination by a physician at the end of the 5 year period or at a later date.

5. The percentage of patients with a microscopically confirmed diagnosis is a measure of the accuracy of diagnosis. This percentage should be as high as possible; patients without a microscopically confirmed diagnosis should be included but shown separately.

6. Whenever possible, an autopsy should be performed. A high degree of accuracy requires that autopsies be performed in the cases of all those patients who die before the end of the 5 year period.

7. The percentage of patients untraced for the full 5 years should be as close to zero as possible. If it is greater than 10 per cent, the report will be of doubtful validity.

8. In reporting on cancer of a given primary site, patients will be classified according to the status of that disease. If a new primary, histologically proved cancer develops, it should be considered as an intercurrent disease even though it may cause the death of the patient.

TREATMENT OF CANCER

The only methods of curing human cancer known today consist of surgically extirpating the growth or destroying it by ionizing radiations. The ancients destroyed cancer either by burning it out or cutting it out and the principles of today are essentially the same but the methodology is highly refined. The final answers for controlling cancer must come from the laboratory, but, while research gains have been great, methods of curing cancer by disrupting its metabolism may not be discovered for years, even centuries. The clinical problem is that of providing adequate treatment of the patient suffering from cancer today and offering him the optimal chance for cure. These are parallel routes of endeavor—basic investigation into the nature of cancer and clinical methods of treating patients with cancer even though its cause and nature is not known. The problem of caring for the cancer patient in 1900 differs markedly from the problem as it exists today. In 1900, practically every patient who bore cancer died from the disease; its diagnosis was a death warrant. Social apathy excluded this disease from the minds of men, and people bearing cancer were classified as having a hopeless condition, were not even permitted access to many hospitals, and were usually cast off to die. The accessible cancers were treated by escharotics. Irradiation which had been discovered just a few years previously was sometimes used empirically for certain accessible cancers. Although certain operations had been described for the treatment of certain cancers (gastrectomy, glossectomy, laryngectomy), the mortality rates were so high that only an occasional bold surgeon would attempt the surgical extirpation.

CANCER CHEMOTHERAPY

The hope of a cancer cure by means of chemotherapy is foremost in the minds of both the public and the medical profession. That cure may someday be accomplished by certain measures is probable, but to predate the time for a given discovery is not only faulty logic but dangerous propaganda. The practices of certain cancer research centers of publicizing each minute shrinkage of a mouse tumor following the administration of a given chemical and of heralding these various laboratory procedures as probably being practicable for the control of human cancer are most pernicious. NO KNOWN HUMAN CANCER CAN BE CURED BY CHEMOTHERAPEUTIC MEASURES. Certain chemical escharotic pastes can control certain cancers and represent the method of the ancients for curing certain cancers. The microscopically controlled chemical method of fixing cancer in vivo and excising this tissue, as practiced by Mohs of Wisconsin, has afforded a means for curing patients with exposed cancers which are locally infiltrative.

Every form of chemical measure for treating cancer has been attempted from the earliest times until the present. Some of these measures included purgatives, blood-letting, weird diets, reptile venoms, heavy metals, and thousands of others. It is lamentable that certain charlatans, both within and outside the medical profession, still practice some of these measures, thereby depriving patients with early cancer a chance for cure.

Chemotherapy, as developed and practiced during the past 50 years, has contributed immeasurably to the cancer problem in many ways. Some of these include:

1. Tools for research into the nature of cancer with a mustering of all the chemical sciences, including immunology. endocrinology, enzymology, and the chemical identification of antitumor derivatives of bacteria and viruses.

2. The curbing of the progression of certain cancers and the marked palliation in patients harboring them (leukemia, and prostatic and breast carcinoma).

3. The release from suffering and the prolongation of life which has served to alter the philosophy regarding cancer. Cancer, even when beyond the stage of complete eradication, is not now regarded as the hopeless, miserable plight that it had been, but may be classified with such conditions as heart disease, cirrhosis, chronic nephritis, and others, of which the patient is never cured but with which he may live pleasantly for prolonged periods. Developments during the past 50 years shall be presented under the heading of the different mechanisms discussed.

Karnofsky and Gellhorn have developed the following framework pertaining to the approaches for cancer chemotherapy:

A. Interference with tumor blood supply by microorganisms
B. Damage to cellular function common to normal and neoplastic cells
C. Alteration of environment of the cancer cell
D. Modification of systemic toxicity produced by cancer

E. Destruction of "neoplastic component" of the malignant cell
F. Stimulation of tissue defenses which limit the growth and spread of malignant cells.

Interference with Tumor Blood Supply by Microorganisms.

At the end of the last century certain observations stimulated the investigation of the bacterial effect upon cancer. Busch, in 1866, reported regression of inoperable sarcomas in 2 patients suffering from erysipelas infection. In 1882, after isolation of the streptococcus which produces erysipelas, Fehleisen reported encouraging results following its injection into cancer patients. Investigation of the carcinolytic effects of bacterial products was started by Spronck in 1892. Interest subsided but was reawakened with the increased investigation of the Arthus phenomenon in 1903 and the description of the Shwartzman phenomenon in 1927. Gratia and Linz studied the effects of bacterial products on tumors in animals extensively. The greatest proponent of cancer therapy with bacterial filtrates was the late William B. Coley who used a filtrate from "Streptococcus erysipelas" and Bacillus prodigiosus from 1891 until 1935. Shear, in 1940, isolated a polysaccharide from culture filtrates of Serratia marcescens, which produces a severe hemorrhagic necrosis in tumors, but it has been shown to be too toxic when administered to human beings.

Spirochetes were claimed to exert a regressive effect in 1910 by Daels and in 1928 by Comsia, but Roskin *et al.* in 1931 revealed no such effect. Attempts to ligate the blood vessels supplying tumors have also been unsuccessful.

Damage to Cellular Function Common to Normal and Neoplastic Cells

Cytotoxic chemicals.

I. Arsenic. Of the numerous metals employed, arsenic (as administered in Fowler's solution) is still used by many to help control leukemic symptoms.

II. Stilbamidine. A compound used for visceral leishmaniasis or kala azar was utilized by Snapper in 1946 for treating multiple myeloma. Its basis was the hyperproteinemia of both diseases, but electrophoretic studies by Gutman *et al.* have shown that there are abnormal plasma proteins in multiple myeloma whereas in kala azar the hyperproteinemia is due to a hypergammaglobulinemia. Severe pain from multiple myeloma can be relieved by stilbamidine, but toxic reactions consisting of damage to the fifth cranial nerve and others caution against its indiscriminate use.

III. Urethane (ethyl carbamate). Haddow and Sexton (1946), in a screening program for chemical carcinolytic agents, noted a marked effect of urethane on experimental animal carcinoma. In the same year it was found to exert a retarding effect in human leukemia (its effect is greater in myeloid than in lymphatic leukemia). In 1947, Huggins reported beneficial effects of this drug on prostatic cancer. Its dangers consist of hematopoietic depression. Haddow and Sexton suggest that the carcinolytic action of this drug might be the result of competition with a natural amine in the biosynthesis of nucleotides.

IV. Nitrogen mustard. Extensive clinical research into the action of mustard gas was started July 12, 1917, when the Germans bombarded the British during World War I and, in addition to other symptoms, leukopenia due to bone marrow depression was described by the Krumbhaars in 1919. Between World Wars I and II the nitrogen analogs of mustard gas, the nitrogen mustards, were developed by European countries, and research concerning their mode of action and prevention of deleterious effects was started by the United States before our entrance into the war. Gilman and Philips summarized the biologic action of some of the nitrogen mustards (betachlorethyl amines and sulfides). Their use for treating cancer was suggested by the marked susceptibility of lymphoid and hematopoietic elements. Although the exact mode of action of the toxin is not known, many believe its action is similar to that of the x-rays. Schrek has demonstrated a different mode of action. Beneficial results following the use of nitrogen mustard have been described for the following entities: Hodgkin's disease, lymphoblastoma, lymphosarcoma, chronic myelogenous leukemia, polycythemia vera, rhabdomyosarcoma, mycosis fungoides, and pulmonary cancer. The chief danger is hematopoietic depression. Klopp, from Washington, D. C., and Bierman, from California, have been able to obtain greater concentrations of nitrogen mustard to the cancer by its administration in arteries supplying the specific tumor. Certain chemical variants of nitrogen mustard have recently been synthesized. Some of these include

triethylene melamine (TEM) which can be administered orally. Triethylene phosphoramide (TEPA) which has been shown to be ineffectual has been replaced by a newer compound, triethylene sulfylamide. Numerous other combinations are now being evaluated.

Antimetabolites. Knowledge concerning the cellular metabolism of cancer, as investigated by Warburg, and the knowledge derived from analysis of mechanisms whereby sulfanilamides exert their antibacterial effect stimulated research to discover methods of inhibiting the metabolism of the cancer cell.

V. Folic acid conjugates. The observation from Lewisohn's laboratory at Mt. Sinai Hospital, in 1938, that an extract of beef spleen and mouse spleen caused regression of mouse sarcoma 180, and extracts of barley and brewers' yeast caused regression of mammary carcinoma in mice, led to the belief that the effective material was a folic acid. This was not confirmed. Farber and his associates, in 1947, published a report that pteroylglutamic acid conjugates (teropterin and diopterin) exerted a cancerolytic effect in man. Gellhorn and Jones state that there is no evidence that teropterin significantly alters the course of malignant neoplasms in man. The Council on Pharmacy and Chemistry of the American Medical Association reached the same conclusion on the basis of reports on 275 patients treated with teropterin and diopterin, but remarked that 50 per cent of the patients enjoyed subjective improvements.

VI. Folic acid analogs. Farber's observation that folic acid conjugates accelerated the course of acute leukemia led to the clinical application of folic acid antagonists. Farber and his colleagues, in 1948, published the results of the folic acid antagonist, aminopterin, in causing temporary remissions in acute leukemia. Use of this drug in acute leukemia in adults also produces remissions but not so impressively as in children. Beneficial results have also been claimed for its use in Hodgkin's disease, lymphosarcoma, and neuroblastoma. Despite the fact that folic acid antagonists were the first drugs to modify the course of acute leukemia in children, they have many drawbacks. Only about one-third have a complete clinical and hematologic remission, about one-fifth show a partial response, and in about 50 per cent the toxic effects vitiate any potential benefit. Patients develop a refractoriness to these drugs. The mechanism for this refractoriness has been investigated by Burchenal and Law and their associates with significant results.

VII. Cortisone and ACTH. Subjective and objective improvement occurs in almost three-fourths of the cases of untreated acute leukemia in children following the use of either ACTH or cortisone. Refractoriness develops rapidly and life is not measurably prolonged. Practically nothing is known concerning the mechanisms by which these hormones produce the remissions.

Alteration of Environment of the Cancer Cell

The clinical application of this principle is the control of disseminated prostatic cancer by hormones. The observation of Gutman and Gutman, in 1938, of a high serum acid phosphatase in patients with disseminated prostatic cancer, and the studies by Gomori in 1941 concerning the distribution of acid phosphatase in normal and neoplastic tissue convinced Huggins that neoplastic prostatic cells might react to the removal of androgenic stimulation. Castration and the administration of estrogens result in subjective and objective improvement and the prolongation of life. With refractoriness to this form of therapy, it is believed that the adrenal glands take over androgenic steroid formation. Accordingly, in 1943, Huggins adrenalectomized patients who had become refractory, with beneficial results.

Modification of Systemic Toxicity Produced by Cancer

Hormones in carcinoma of the female breast. Leo Loeb, in 1919, first demonstrated that castration of female mice with a high incidence of mammary cancer significantly reduced the frequency of the occurrence of the tumor. Androgenic administration to animals with breast cancer and its administration to patients in smaller doses by Farrow and Woodard failed to reveal any beneficial response. Herrmann was the first to demonstrate a beneficial response with larger doses (300 mgm. per week). In a recent Subcommittee Report of the Council on Pharmacy and Chemistry of the American Medical Association, an analysis of 450 patients with advanced breast cancer treated with androgens showed that 80 per cent experienced improvement in their condition, most marked in those with osseous metastases. Estrogens were utilized to treat disseminated breast cancer in postmenopausal women on the basis of producing a hormonal imbalance.

Hypercorticism due to the administration of ACTH or cortisone may exert its effect by modifying the systemic effects produced by cancer as well as by altering cellular function.

Destruction of "Neoplastic Component" of the Malignant Cell

Gellhorn points out that this "neoplastic component" is a highly speculative entity and its definition must precede its destruction or modification.

Stimulation of Tissue Defenses

Again Gellhorn points out that the evidence for inherent defense mechanisms against human cancer is tenuous. The occasional spontaneous regression of a cancer or the disappearance of metastasis after removal of the primary cancer bears evidence to the existence of some defense mechanism. The not infrequent latent period before certain metastases grow and become clinically manifest after the treatment of the primary tumor (breast cancer manifesting itself 10 to 15 years after mastectomy) demonstrates either a resurgence of the growth potential of the latent cancer cell or a breakdown of the host's inhibiting mechanism against the growth of the cancer cell. The belief that the reticuloendothelial system controls this mechanism, and attempts to stimulate the system with antireticular cytotoxic serum, or to stimulate its function with splenic extracts, have proved worthless.

RADIATION THERAPY OF CANCER

One of the greatest discoveries for treating cancer occurred slightly over half a century ago when Röntgen, in 1895, discovered the roentgen rays. Surgery is the only science which exceeds in importance the science of radiation therapy for curing cancer. Irradiation is superior for treating certain cancers, and is of far greater importance in the control of cancer which cannot be completely eradicated, and as a means of offering palliation to patients suffering from widespread cancer.

It is difficult for us today, surrounded as we are by a great science of radiation physics and radiation biology, to look back to a period of slightly over half a century ago at which time the phenomenon of x-radiation was unknown to man. An attempt to trace the chronologic development from the time that Röntgen first discovered the x-rays to the present with our extensive knowledge pertaining to this field of physical phenomena would indeed be impossible. We shall present certain of the highlights pertaining to the widespread application of the rays first discovered by Wilhelm Conrad Röntgen in November of 1895 and presented by him in a preliminary paper on December 28, 1895. The public mind was ready to accept this new discovery, and 23 days after the newspaper announcement (January 6, 1896) of the discovery of the new rays, T. Glover Lyon, in a letter to the London *Lancet*, suggested that they might be used for the destruction of the tubercle bacillus. Credit for their use in the treatment of cancer has been accorded to Grube—not a physician but a manufacturer of Crookes tubes. It is stated that he used them for the treatment of a carcinoma on January 29, 1896, less than a month after the newspaper report of their discovery, which was published even before Röntgen gave his first public address on the subject on January 23, 1896. Thus, x-ray therapy of cancer started almost simultaneously with the discovery of the x-rays.

The enthusiastic use of the x-rays for diagnostic and fluoroscopic purposes resulted in extensive exposure to the rays. This was particularly observed with the production of dermatitis and the production of alopecia following exposure of the scalp. In 1896, Stevens, Feilchenfeld, and Crocker each published opinions on "sunburn" caused by roentgen rays. Gilchrist, at Johns Hopkins Hospital in 1897, collected a series of 23 such cases from the literature and Pfahler states that by 1900, 170 instances of roentgen ray injuries were collected which specifically demonstrated the biologic effect as a result of exposure to radiations. The early observers classified the immediate reactions from irradiation as first, second,

FIG. 10. Development of contrast media for roentgen diagnosis. Diagrammatic representations of the chronologic evolution of the contrast materials used for roentgen diagnosis. a, Only certain of the body systems and organs are shown in this posteroanterior projection. The name of the procedure, the name of the material, the year it was first used, and the method of introduction are given. Symbols are as follows: *D*, direct injection by needle, catheter, or tube; *O*, oral route: *I.V.*, intravenous route. Obsolete contrast media are indicated by light-faced type; media still in use by heavier type. b, The body systems and organs not exhibited in a, are shown in this anteroposterior projection. The additional symbol *I. S.* designates the intraspinal route. Obsolete procedures are so indicated specifically. (L. G. Rigler. *Outline of Roentgen Diagnosis*. J. B. Lippincott Company.)

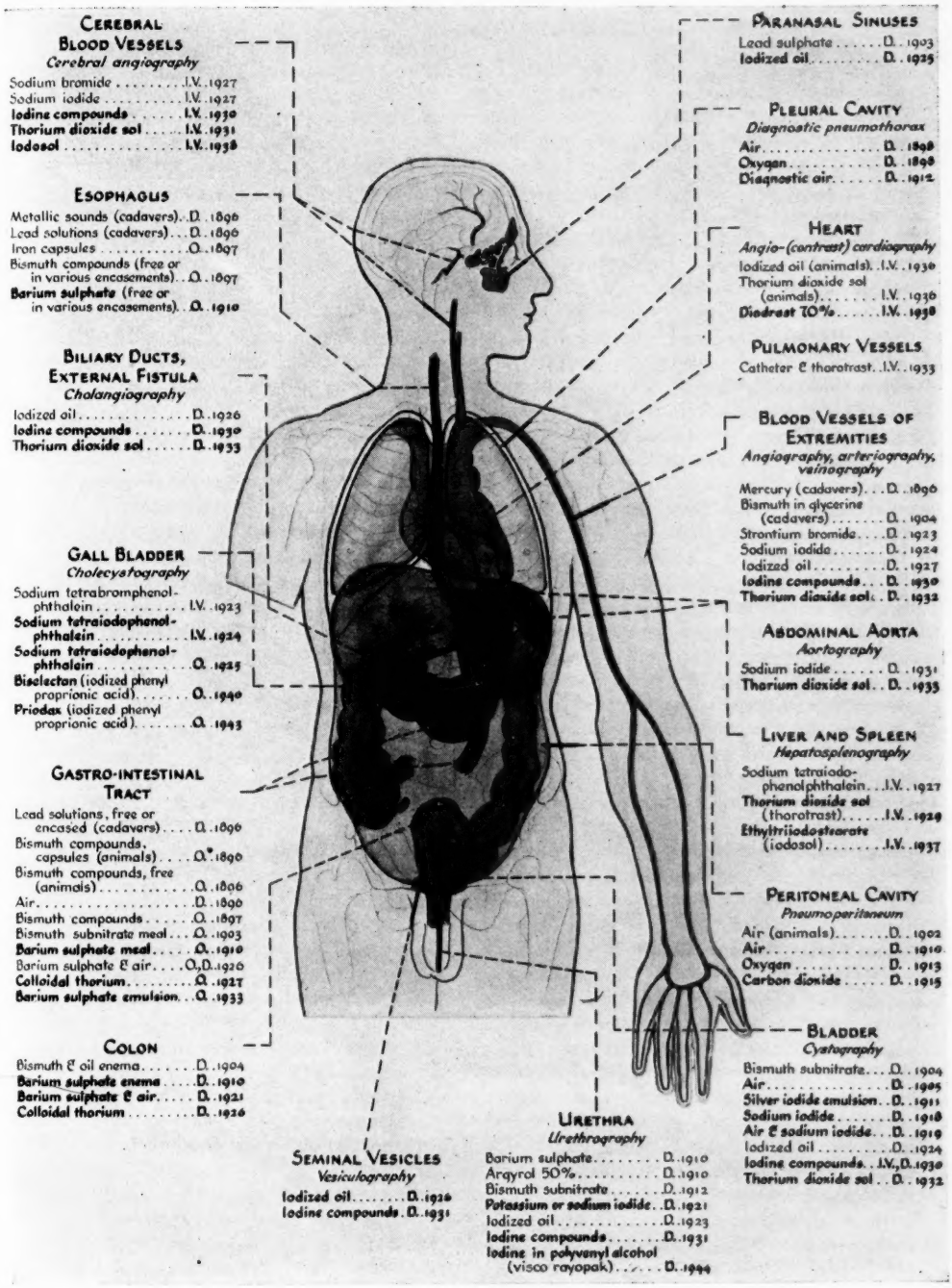

CEREBRAL BLOOD VESSELS
Cerebral angiography
Sodium bromide ..... I.V. 1927
Sodium iodide ..... I.V. 1927
Iodine compounds ..... I.V. 1930
Thorium dioxide sol ..... I.V. 1931
Iodosol ..... I.V. 1938
ESOPHAGUS
Metallic sounds (cadavers) .. O. 1896
Lead solutions (cadavers) ... O. 1896
Iron capsules ..... O. 1897
Bismuth compounds (free or in various encasements) .. O. 1897
Barium sulphate (free or in various encasements) .. O. 1910
BILIARY DUCTS, EXTERNAL FISTULA
Cholangiography
Iodized oil ..... D. 1926
Iodine compounds ..... D. 1930
Thorium dioxide sol ..... D. 1933
GALL BLADDER
Cholecystography
Sodium tetrabromphenolphthalein ..... I.V. 1923
Sodium tetraiodophenolphthalein ..... I.V. 1924
Sodium tetraiodophenolphthalein ..... O. 1925
Bisolectan (iodized phenyl proprionic acid) ..... O. 1940
Priodax (iodized phenyl proprionic acid) ..... O. 1943
GASTRO-INTESTINAL TRACT
Lead solutions, free or encased (cadavers) .... O. 1896
Bismuth compounds, capsules (animals) .... O. 1896
Bismuth compounds, free (animals) ..... O. 1896
Air ..... O. 1896
Bismuth compounds ..... O. 1897
Bismuth subnitrate meal ... O. 1903
Barium sulphate meal ..... O. 1910
Barium sulphate & air .... O, D. 1926
Colloidal thorium ..... O. 1927
Barium sulphate emulsion .. O. 1933
COLON
Bismuth & oil enema ..... D. 1904
Barium sulphate enema ..... D. 1910
Barium sulphate & air ..... D. 1921
Colloidal thorium ..... D. 1926
PARANASAL SINUSES
Lead sulphate ..... D. 1903
Iodized oil ..... D. 1925
PLEURAL CAVITY
Diagnostic pneumothorax
Air ..... D. 1898
Oxygen ..... D. 1898
Diagnostic air ..... D. 1912
HEART
Angio-(contrast) cardiography
Iodized oil (animals) .. I.V. 1930
Thorium dioxide sol (animals) ..... I.V. 1936
Diodrast 70% ..... I.V. 1938
PULMONARY VESSELS
Catheter & thorotrast .. I.V. 1933
BLOOD VESSELS OF EXTREMITIES
Angiography, arteriography, vainography
Mercury (cadavers) ... D. 1896
Bismuth in glycerine (cadavers) ..... D. 1904
Strontium bromide .... D. 1923
Sodium iodide ..... D. 1924
Iodized oil ..... D. 1927
Iodine compounds ... D. 1930
Thorium dioxide sol .. D. 1932
ABDOMINAL AORTA
Aortography
Sodium iodide ..... D. 1931
Thorium dioxide sol .. D. 1933
LIVER AND SPLEEN
Hepatosplenography
Sodium tetraiodophenolphthalein ... I.V. 1927
Thorium dioxide sol (thorotrast) ..... I.V. 1929
Ethyltriiodostearate (iodosol) ..... I.V. 1937
PERITONEAL CAVITY
Pneumoperitoneum
Air (animals) ..... D. 1902
Air ..... D. 1910
Oxygen ..... D. 1913
Carbon dioxide ..... D. 1915
BLADDER
Cystography
Bismuth subnitrate ... O. 1904
Air ..... D. 1905
Silver iodide emulsion .. D. 1911
Sodium iodide ..... D. 1918
Air & sodium iodide ... D. 1919
Iodized oil ..... D. 1924
Iodine compounds .. I.V., D. 1930
Thorium dioxide sol .. D. 1932
URETHRA
Urethrography
Barium sulphate ..... D. 1910
Argyrol 50% ..... D. 1910
Bismuth subnitrate ..... D. 1912
Potassium or sodium iodide .. D. 1921
Iodized oil ..... D. 1923
Iodine compounds ..... D. 1931
Iodine in polyvanyl alcohol (visco rayopak) ..... D. 1944
SEMINAL VESICLES
Vesiculography
Iodized oil ..... D. 1926
Iodine compounds .. D. 1931

Fig. 10a.

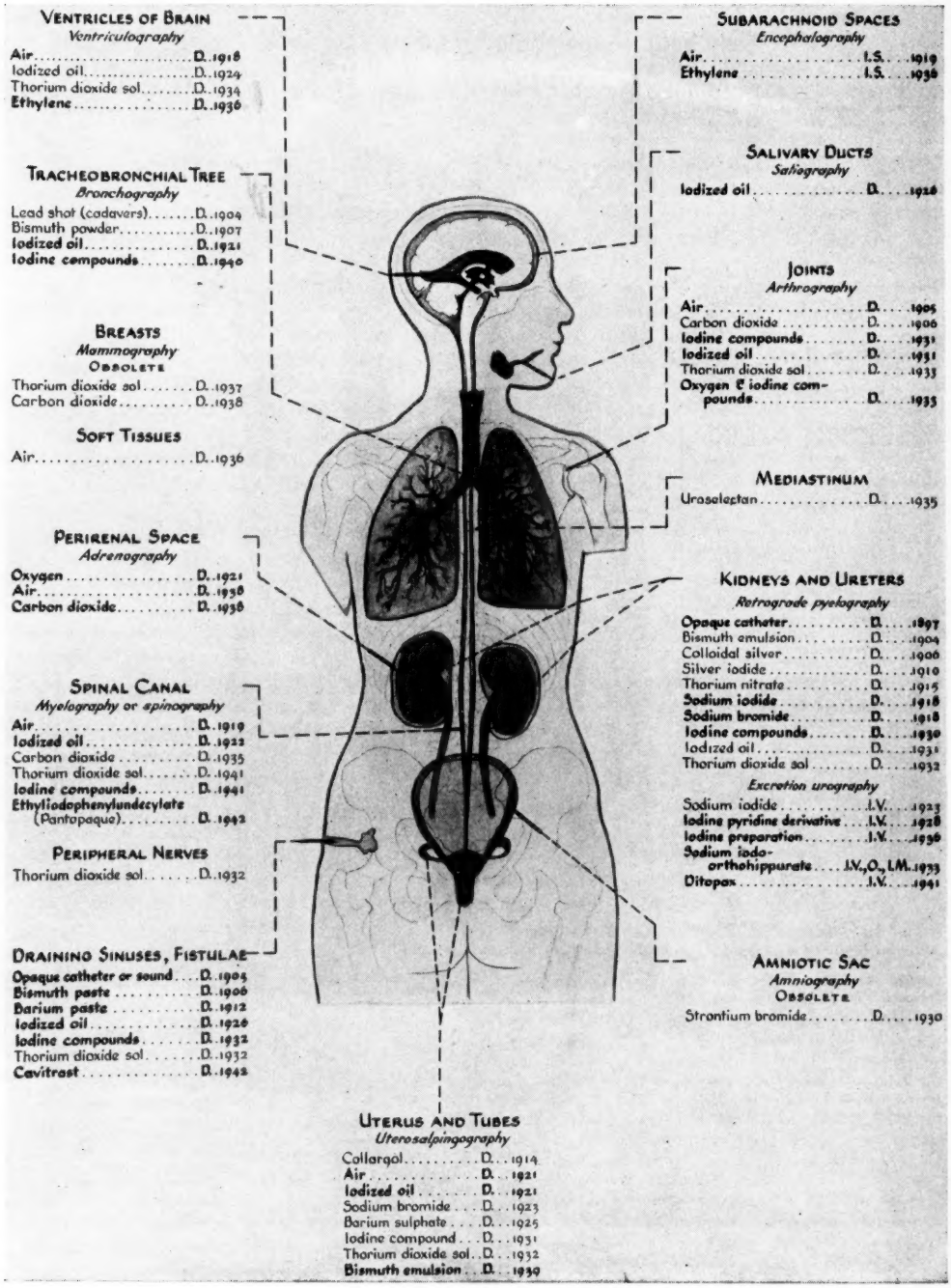

VENTRICLES OF BRAIN
Ventriculography
Air D. 1918
Iodized oil D. 1924
Thorium dioxide sol D. 1934
Ethylene D. 1936
TRACHEOBRONCHIAL TREE
Bronchography
Lead shot (cadavers) D. 1904
Bismuth powder D. 1907
Iodized oil D. 1921
Iodine compounds D. 1940
BREASTS
Mammography
OBSOLETE
Thorium dioxide sol D. 1937
Carbon dioxide D. 1938
SOFT TISSUES
Air D. 1936
PERIRENAL SPACE
Adrenography
Oxygen D. 1921
Air D. 1936
Carbon dioxide D. 1938
SPINAL CANAL
Myelography or spinography
Air D. 1919
Iodized oil D. 1922
Carbon dioxide D. 1935
Thorium dioxide sol D. 1941
Iodine compounds D. 1941
Ethyliodophenylundecylate (Pantopaque) D. 1942
PERIPHERAL NERVES
Thorium dioxide sol D. 1932
DRAINING SINUSES, FISTULAE
Opaque catheter or sound D. 1905
Bismuth paste D. 1906
Barium paste D. 1912
Iodized oil D. 1926
Iodine compounds D. 1932
Thorium dioxide sol D. 1932
Cavitrast D. 1942
SUBARACHNOID SPACES
Encephalography
Air I.S. 1919
Ethylene I.S. 1938
SALIVARY DUCTS
Sialography
Iodized oil D. 1928
JOINTS
Arthrography
Air D. 1905
Carbon dioxide D. 1906
Iodine compounds D. 1931
Iodized oil D. 1931
Thorium dioxide sol D. 1933
Oxygen & iodine compounds D. 1935
MEDIASTINUM
Uroselectan D. 1935
KIDNEYS AND URETERS
Retrograde pyelography
Opaque catheter D. 1897
Bismuth emulsion D. 1904
Colloidal silver D. 1906
Silver iodide D. 1910
Thorium nitrate D. 1915
Sodium iodide D. 1918
Sodium bromide D. 1918
Iodine compounds D. 1930
Iodized oil D. 1931
Thorium dioxide sol D. 1932
Excretion urography
Sodium iodide I.V. 1923
Iodine pyridine derivative I.V. 1928
Iodine preparation I.V. 1930
Sodium iodo-orthohippurate I.V., O., I.M. 1933
Ditopax I.V. 1941
AMNIOTIC SAC
Amniography
OBSOLETE
Strontium bromide D. 1930
UTERUS AND TUBES
Uterosalpingography
Collargol D. 1914
Air D. 1921
Iodized oil D. 1921
Sodium bromide D. 1923
Barium sulphate D. 1925
Iodine compound D. 1931
Thorium dioxide sol D. 1932
Bismuth emulsion D. 1939

Fig. 10b.

and third degree erythemas, and the chronic cases produced the well known atrophy, telangiectasis, hyperkeratosis, warts, fissures, ulcerations, and the ultimate carcinoma.

The epilating effects of x-rays described by Daniel of Vanderbilt University and Marcuse of Berlin led Freund, in 1897, to use the new rays in treating a young girl with a disfiguring hairy nevus. The result was reported as good, and the wide publicity which its use engendered led to its enthusiastic application, especially for skin diseases. Sjorgren and Stenbeck (1899) first treated epitheliomas; Scholtz (1902) treated mycosis fungoides, and Pusey and Senn, in 1903, treated leukemia and lymphadenoma.

The early equipment was extremely simple. Ruhmkorff or Tesla coils or a static machine produced the necessary high tension, and a Crookes tube produced the radiation. The tube was bare, with no protection whatsoever to either the patient or the operator, which resulted in radiation damage to both. There were no methods of measuring either the radiation or the amount of electricity. Volt meters and milliampere meters were not available. Voltage was estimated by the distance between spark gaps, and the intensity of the current and the penetrative quality of the rays were judged by the appearance of the hand held in front of the fluoroscope. This led to the loss of hands and fingers by many of the early workers in the field. The discovery of the ammeter and milliampere meter (d'Arsonval) led to a method of measuring currents and voltages.

The first great step in the production of the higher voltages was that by Snook, in 1905, who discovered the interrupterless coil which consisted of a motor-driven, rotating, high tension switch by which the higher voltage portion of the sine wave was reversed once it carried the high tension current into the tube in one direction. This permitted a markedly improved form of current, but it remained for Coolidge to develop the hot cathode tube in 1913. This was the development of a vacuum tube which, although changed to meet present requirements, remains standard today in principle and even in design.

An exciting story regarding the development of the Coolidge tube has been published by Coolidge in the November, 1945 issue of *Radiology* which commemorates the half century of progress since the discovery of the roentgen ray.

Development of Radiation Dosimetry

The earliest methods of measuring the quantity of radiation were developed at the turn of the century. Quimby has reviewed the historical development of radiation dosimetry in the December 1945 issue of the *American Journal of Roentgenology* from which some of the subsequent data have been obtained. The accurate measurement of the quantity of radiation is stressed because it marks the transition between the empirical and rational basis for radiation therapy. In 1902, Holzknecht described pastille radiometers which measured radiations as a result of change in color of various organic compounds. Following their use, fluorescent standards became popular, being utilized by Contremoulins (1902) and by Wintz and Rump who developed (1926) a precision instrument by which the photometer would measure the intensity of fluorescent light induced by the radiation.

Then followed a photographic radiometer, apparently first described by Stern, and developed to a high degree of usability. Following this, the observation that selenium exerted electrical resistance under the action of either light or roentgen rays led to the utilization of the selenium cell as a method of measuring radiation. The Furstenau intensimeter, developed in 1915, was actively used for many years.

Shearer, in 1915, developed a formula for computing radiation which was extensively utilized, especially by dermatologists. His method was based on the observed facts that (a) the intensity varies directly with the milliamperage, (b) the intensity varies directly with the square of the voltage (this is accurate only within a very limited range), and (c) the intensity varies inversely as the square of the distance from the target to the skin.

The ionization method of measuring the quantity of radiations. It is of interest that Röntgen in his first article described the fact that radiation would produce ionization, and electroscopes and electrometers based on this principle were used by the earliest workers in the field of radiation, including the Curies, Geitel, Wilson, and others. However, their use was discontinued and, according to Quimby, the first reference in the literature to their renewed use was in an article written in 1905 by Milton Franklin who advocated the use of a metal box containing an aluminum fiber on a metal post and an electrostatic

charging device. Physicists throughout the world recognized the advantage of this form of measuring the quantity of radiation, and Villard, in 1908, designed a combined ionization chamber and electrometer. A few years later Szilard made very critical measurements and strongly advocated the utilization of ionization chambers as a means of measuring the quantity of radiation. In Germany, the physicists proposed the unit described by Villard and utilized by Behnken, and this was adopted by the German Roentgen Ray Society. In Francê the Solomon unit, R, was the one accepted. In Sweden, Sievert and his associates at Radiumhemmet described a unit which was widely used; in the United States, Duane, Failla, Weatherwax, Quimby, and others developed instruments to measure ionization.

At the Second International Congress a few years later, several critical papers were presented, especially one by Failla in which he gave an accurate definition of the unit for measuring the quantity of radiation and described methods of measuring it. At the Fourth International Congress in Switzerland, in 1934, attempts were made to broaden the unit so that it would include gamma rays. In Chicago, during the Fifth International Congress, the International Unit was described as follows: "(1) The International Unit of quantity or dose of x-rays or gamma rays shall be called the 'roentgen' and shall be designated by the symbol 'r,' (2) the roentgen shall be the quantity of x or gamma radiation such that the associated corpuscular emission per 0.001293 gram of air produces, in air, ions carrying 1 e.s.u. of quantity of electricity of either sign."

With the establishment of these definitions, the question of clinical dosimetry became important, particularly because of the failure of agreement of the various ionization chambers used in various countries to measure the same thing. This was largely settled as recently as 1930 when Lauriston Taylor at the United States Bureau of Standards devised a guarded field standard ionization chamber that made it possible to construct a standard instrument in portable size. He took his apparatus throughout France, England, and Germany, and at last agreement was reached as to the method of measuring. Thus, from the physical standpoint, the roentgen "is now an accurately established unit" (Quimby).

Clinical dosimetry. The need to translate the physical measurements into units of energy as they affect the body in different depths became one of absolute importance. The Compton and photoelectric effects, the result of secondary electrons, must be interpreted on the basis of the total dose. The effects of filtration upon the beams become important, and it is of interest in this respect that Röntgen, in his third paper, in 1897, stated, "If we imagine a substance divided into layers of equal thickness, placed perpendicular to parallel rays, each of these layers is more transparent for the transmitted rays than the one before it." The first mention of target-skin distance found in the literature is stated by Quimby to be that of Williams in 1903. With the necessity for measuring the effects of rays as they pierce the tissues, phantoms were constructed and measurements were made in these phantoms by means of various ionization chambers. As a means of expressing these dosages, Friedrich and Glasser coined the term "isodose charts" to show the distribution of radiation about radium sources, and these were adapted to roentgen rays and carefully investigated by Failla, Weatherwax, Glasser, and others. In order accurately to calibrate the various small ionization chambers within tissue, Failla constructed the extrapolation ionization chamber which made possible absolute measurement of tissue dose both at the surface and within the depth of the phantom. Thus, methods are now available which rather quantitatively measure not only the amount of radiation as it is delivered from the tube, but also the quantity of radiation as it exists in a given depth within the body.

Attempts are now being made to translate these values into the absolute energy in existence within a given site within the body and to express the measures in ergs, a unit of measure of energy. This becomes particularly important for energies above 3,000,000 electron volts.

The observations that such physical factors as voltage, amperage, filtration, target-skin distance, and size of portal affect not only the quantity of radiation but also produce a polychromatic ray made necessary instruments to measure the type of ray being produced under a given circumstance. Here again Röntgen, whose original observations included almost the entire field of the physical characteristics of the x-rays, made a notation concerning the quality of radiation when he stated that the greater the length of the parallel spark gap, the more penetrating the x-ray beam, and he performed a series of studies

on the penetration of the x-ray beam by means of a platinum-aluminum window.

The concept of half-value layer was introduced by Christen in 1912 as a measure of quality. Various filters have been advocated, including aluminum, copper, and the Thoraeus filter. In the United States the description of voltage by means of an equivalent spark gap was employed regularly and served its purpose for a given period; however, with refinements of techniques and methods its use has been discarded.

The utilization of spectrographic methods of measuring x-rays was carried on, and the Seeman spectrometer, which measured the minimum wave length, was used rather extensively although it had shortcomings. Duane utilized the effective wave length, and since then suggestions have been presented for the utilization of the average wave length, average absorption coefficient, and others. Taylor and Singer, in 1934, advocated a different approach when they made absorption curves in aluminum and copper for roentgen rays produced at a definite constant potential. Thus, a full absorption curve taken for any beam could be compared with the standard series and its constant equivalent potential determined. At the Fifth International Congress of Radiology, the specification made concerning the quality of radiation reads as follows: "For most medical purposes, it is sufficient to express the quality of x-radiation by the half-value layer in a suitable material: up to 20 kv. (peak) cellophane or cellone; 20–120 kv. (peak) aluminum; 120–140 kv. (peak) copper; 400 kv. up (peak) tin. For a more definite specification of the quality of the radiation the complete absorption curve in the same material is preferable."

Attempts to define the quality of radiation at given depths within the tissue, which of course alters as the beam penetrates the tissue, were made by Quimby and McNattin in this country, and Clarkson and Mayneord in England, and valuable data have thus been obtained. Numerous investigators have attempted to measure biologic effects and interpolate these to a given physically measured dose. Thus, Glocker and his associates measured bean roots; Holthusen measured Ascaria eggs; Wood and Packard, Drosophilia eggs; and Henshaw, various seeds and eggs. The study of recovery as it relates to erythema production was carefully measured by Quimby and MacComb.

Biologic Effects of Ionizing Radiations

The early application of roentgen rays to the biologic system necessitated a study pertaining to the biologic effects of radiation. The earliest such study recorded was performed before the turn of the century by Elihu Thomson, who proved that the dermatitis developed only in that part of the body actually exposed to the rays. The great study concerning the biologic effects of radiation was started by Kienböck in 1900 when he irradiated rats enclosed in metal cylinders to exclude light and electrical effects, and proved that the effects were the direct results of the rays. Kibbe and Gilchrist, in 1897, separately published articles describing the histologic effect of the rays on the skin and, in 1903, Albers-Schoenberg produced aspermia in experimental animals without injury to the overlying skin. This was the first study demonstrating a selective sensitivity of different cells to irradiation. The great studies performed by Bergonie and Tribondeau in 1904 completely depicted the histologic picture of the changes produced by irradiation of rat testicles and showed that the focus of attack was upon the embryonic structures. The law of Bergonie and Tribondeau was thus formulated. This states: "Immature cells and cells in an active state of division are more sensitive to radiation than are cells which have already acquired their adult morphological and physiologic character." Further investigations confirmed the findings of Bergonie and Tribondeau.

Lacassagne, from 1910 on, carefully studied the biologic effects of radiation, and in a book by him published in 1941 he summarized his findings, as well as the biologic effects observed by others. Some of his early observations related to the effects of the ion upon the cells, dependent upon the spatial site of the impact of the ion in addition to the ionic mass. Several results occurred, and included in these are immediate death due to massive destruction of the cell, impaired growth and partial damage, suppression of reproduction due to destruction of the centriole, abnormal anomalies associated with division due to destruction of the nuclear chromatin, and, if the genes were the target, hereditary malformations.

The effects upon single-celled animals were compounded in geometrical proportions when attempts at their analysis were carried to the

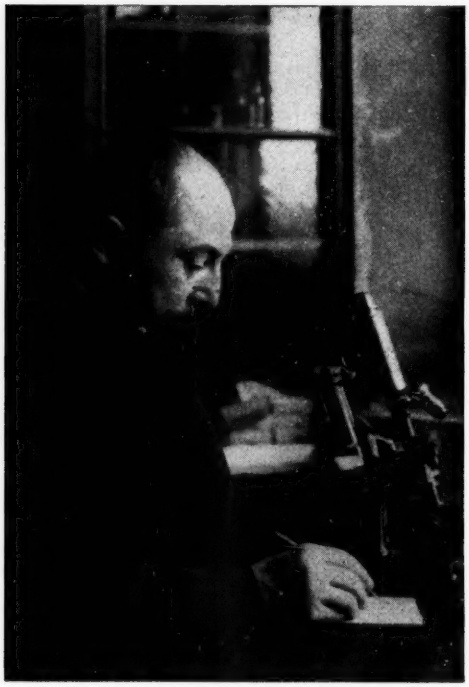


FIG. 11. Claude Regaud.

multicellular animals. These studies have been summarized by Zirkle who, in 1949, published a provocative article entitled, "Relationships Between Chemical and Biologic Effects of Ionizing Radiation." In this article he called attention to numerous observations which indicate that not only do various organs respond to irradiation because of their inherent radiosensitivity but also because of other factors which include effects upon the blood supply, alterations in the connective tissue with the production of fibrosis, alterations in the fluidity of the system, and other changes of an unknown nature.

The nature of oxygen and its effect upon irradiated systems have been investigated since the earliest days of the century. Loiseleur (1953) has recently summarized the effects of irradiation, demonstrating that the reactivation of liberated oxygen increases in irradiated tissues and may be an important factor in radiation effects. The liberation of nascent oxygen has been considered to be a cause of radiation sickness, and recently (1950) Dowdy has demonstrated that the production of anoxia in animals receiving irradiation will be protective against the lethal effects of irradiation. The question of radiosensitivity of tissue is one which is difficult to define and which has been extensively investigated.

The effects of irradiation upon various organs of the body have been carefully investigated, especially by Whipple and Warren, and numerous articles have been written upon this subject. Explanation of reactions and identification of alterations produced by irradiation upon the various chemical constituents of the cells, upon the enzymatic systems in the cells, and upon other systems in the body, are being sought intensively by investigation. The renewed interest in this subject as a result of the application of atomic energy has been summarized in a two volume book by Hollaender (1954) which has been published under the auspices of the National Research Council. Hollaender mentions that, despite the voluminous amount of literature on this subject, an understanding of the actual effects of ionizing radiations upon biologic systems remains enigmatic.

Use of Radiotherapy in the Treatment of Cancer

From the beginning phase in which use of ionizing radiation to treat cancer was based purely on empiric grounds, the science of radiotherapy has developed so that the art of its application has cured many cancers and yielded significant palliation to patients whose cancers were beyond the realm of complete cure. Some tumors such as lymphosarcomas, transitional cell carcinomas and lymphoepitheliomas, seminomas, myelomas, Ewing's sarcomas, and certain epidermoid carcinomas respond remarkably well to radiation therapy. For others which are moderately radiosensitive, such as most of the epidermoid and basal cell carcinomas of the skin, mucous membranes, cervix, and larynx, radiation therapy may cure the patient if it is administered properly and the neoplasm remains localized. In these instances the choice between radiation therapy and surgery depends upon many other factors. Even radioresistant tumors such as certain sarcomas are sometimes cured by radiation therapy when the patient refuses surgical intervention. The response to radiation therapy of leukemia, polycythemia vera, diffuse myeloma, and diffuse metastases from breast and prostatic cancer is well known. Certain inoperable tumors are sometimes rendered operable by a course of radiation therapy.

Techniques of Roentgen Therapy

The fact that there were no methods of measuring dosages of irradiation necessitated the administration of roentgen therapy in small daily dose units, the total dose being determined by the total tissue changes.

Kingery, in 1920, attempted to organize this fractional dose technique by employing a system which he designated as the "saturation" method. This consisted of delivering a dose of x-rays necessary to produce an erythema and then maintaining this effect for a given period by the administration of smaller doses. In the same year, Seitz and Wintz advocated the massive dose technique which was the administration of a "carcinoma" or "sarcoma" dose in the shortest period possible. Good results were recorded, especially in Europe, but the technique never became accepted in America and is practically never utilized now. Recently, research into this technique was advocated by Friedman of New York.

The preceding dose schedules were based upon empiricism. About 1914, Regaud, who had done intensive studies on the effects of small doses of irradiation extended over a long time, noticed that the most pronounced effects occurred during the phases of mitosis, at which time the cells were most sensitive to the destructive effects of irradiation. He accordingly advocated the administration of roentgen rays over a prolonged period in order to strike the cells when they were most susceptible to the irradiation. In 1920, Coutard, who was associated with Regaud at the Curie Institute, applied these principles with modifications to the treatment of cancer about the head and neck, especially about the larynx. The application of this method has come to be known as the Coutard method. He originally irradiated the region daily or twice daily with small doses of heavily filtered radiations generated at high voltages (200 kv.). Later the dose was "diluted" by increasing the filtration, decreasing the milliamperage, and increasing the distance, until at times 1 or 2 hours or more were necessary to deliver 150 to 180 roentgens. A course of therapy lasted from 3 to 6 weeks. A careful review of the results obtained by this method was performed by Schinz, who had practiced the use of Coutard's fractionated method over a period of 17 years and published his results in 1937.

FIG. 12. Henri Coutard.

Radium Therapy

Henri Becquerel, in 1896, in an attempt to ascertain whether ordinary bodies emitted irradiation similar to that discovered by Röntgen, exposed a number of phosphorescent substances enveloped in black paper under a photographic plate but with negative results. However, when he carried out this procedure with uranium salts the photographic plate revealed a complete photograph. In 1898, Pierre Curie and Marie Sklodowska Curie separated from pitchblende the unknown element they called radium. S. W. Goldberg and E. S. London, in 1903, observed that when Goldberg applied radium to his own forearm, a slowly healing ulcer developed. Suspecting that radium would have an effect on cancerous epithelium these investigators treated 2 basal cell carcinomas of the face; both healed with a good cosmetic result. In 1902 Morris Manges and Willy Meyer purchased from the Curie Clinic 4.25 mgm. of radium bromide. They first treated a large, hairy congenital nevus of the chest which had recurred 2 months after radical excision; no beneficial effect resulted

from the radium. In 1903 Robert Abbe purchased from the Curie Laboratory 150 mgm. of radium bromide ($400) and experimented on germinating seeds, ants, trout, polywogs, mice, and normal human skin. He also treated a breast cancer. With this early beginning, there developed the great science of radium therapy. Large centers were established, such as the Curie Institute in Paris, Radiumhemmet in Sweden, the large clinics in England (notably the one in Manchester), and the Memorial Hospital in the United States. Coincident with the establishment of these institutions a co-ordinated effort between the physician and physicist occurred and pioneers—Lacassagne, Berven, Janeway, Failla, Quimby, *et al.*—developed the physical and biologic science of radium therapy for cancer. In America the Memorial Hospital Group experimented with interstitial radium. Failla developed an apparatus for collecting radon, utilizing the mercury pump and Torricelli vacuum. Experiments first with glass radon seeds and later with gold-filtered radon seeds established a standard method for interstitial irradiation. The necessity of accurate dosimetry stimulated practical research in this field. The tables formulated in England by Paterson and Parker, and those in America by Quimby for calculating isodose curves for radium usage have become standard.

Radium dosage in earlier years was measured in terms of milligram hours, or millicuries destroyed, but now the interpolation of radiation dose in terms of gamma ray roentgens better serves to standardize the methods of dosimetry for radium therapy. The division of radium therapy into teleradium therapy, intracavitary therapy, mold therapy, and interstitial therapy further subdivides the special problems peculiar to radium, a naturally occurring radioactive isotope. Today radium is more widely used in Europe than in America. The use of radium in conjunction with x-rays for the treatment of cancer of the cervix represents an example of the combined use of two forms of radiation sources for eradicating a given cancer. Each form of radiation contributes its specific benefit in controlling the cancer.

Rotation Roentgen Therapy

Rotation roentgen therapy is a method of distributing the incident beam over a large surface area wherefrom very little effect occurs on one surface of the body but a cancercidal dose of roentgen rays is delivered to lesions situated deeply within the body. It actually represents an expansion of the multiple port technique by cross-firing through an infinite number of portals. In 1906, Pohl first suggested the advantages of rotation roentgen therapy and more recent exponents of this form of therapy are DuMesnil de Rochemont (1937), Flax (1937), Dessauer, Lion, and Gokmen (1937), Nielsen (1945), Hawley (1948), Green (1949), Hare *et al.* (1951), and Kligerman and Schaefer (1952).

Two methods of rotation therapy are: (1) rotation of the tube about an immobile patient, and (2) rotation of the patient about a fixed beam of roentgen rays as on a turntable. Various forms of apparatus have been developed to accomplish this, and more recently Trump, Master, and Cloud (1947) devised a mechanism for delivering supervoltage x-irradiation by the rotation therapy technique. The results are promising as this technique offers a distinct advantage as a means of delivering large doses to deep-seated cancers with minimum effect upon the surface.

Supervoltage X-ray Therapy

Supervoltage x-ray therapy was first inaugurated in 1932. In 1935, Stone, Livingston, Sloan, and Chaffee built a milllon volt generator. Physical investigation indicated that this method had advantages over deep x-ray therapy for at least three reasons as outlined by Leucutia: (1) it permitted the administration of a certain physical dose to cancer with less effect on the skin; (2) it made possible a more homogeneous irradiation, especially of large volumes of tissue, because of the greater depth dose and lesser attenuation of the beam; and (3) it permitted a simplification of radiation by reducing the number of portals necessary for the purpose of cross fire.

Various reviews in the literature attest to the efficacy of supervoltage x-ray therapy but demonstrate no sharp and extensive advantage over conventional x-ray therapy at 220–250 kv. Schmitz in 1943 recorded the cases of 72 patients with cancer of the cervix treated by supervoltage x-ray therapy with 37.5 per cent 5 year cure, which was an improvement over ordinary x-ray therapy in their experience. Kamperman, in 1941, also reported an improved salvage rate. Colby and Schulz, in 1943, reported on 139 bladder cancers treated by supervoltage x-ray therapy and indicated a 40 per cent 4-year survival, as compared with 20 per cent prior to the institution of supervoltage x-ray therapy. Philips, reporting

from St. Bartholomew's Hospital in London, described advantages of supervoltage therapy for treating cancer of the cervix, larynx, and especially cancer of the rectum. Watson and Urban reported on 63 patients with intrathoracic cancer, and Hooker and Guttmann reported on 315 various types of cancer that revealed no great benefits from supervoltage irradiation. Holmes and Schulz, in 1946, reviewed 1,835 cases of cancer treated with supervoltage x-ray from 1937 to 1944; e.g., they described the cutaneous advantage and good immediate palliation and observed a slight but definite increase in life expectancy. Leucutia, reporting on various forms of cancer treated by supervoltage x-ray therapy, also has noted an improvement in 5 year survival rate and increased palliation. Thus, supervoltage therapy may be considered an added refinement to radiation therapy, but no revolutionary improvement. Cancers which are resistant to the conventional deep x-ray therapy are also resistant to supervoltage therapy.

The Betatron

The betatron, which was first described by Kerst in 1941, represents a type of electron accelerator which can generate and eject electrons theoretically up to hundreds of millions of volts. The one developed by Kerst and utilized by Roger Harvey in the treatment of cancer generates 20,000,000 electron volts. This apparatus is being utilized with apparent success in the treatment of cancer and represents a present day method of investigation.

The Cyclotron; Utilization of Its Products in Cancer Therapy

The construction of the cyclotron from spare parts of a Navy transmitter by Ernest Orlando Lawrence at the University of California in 1932 represents a hallmark in the development of a method of accelerating atoms and made available a method of producing, artificially, radioactive isotopes.

The great discoveries at the end of the last century, which include Röntgen's discovery of x-rays, Becquerel's discovery of radioactivity a year later, Thomson's isolation of the electron in 1897, and Curie's discovery of polonium and radium in 1898 represent the beginning of diagnostic and therapeutic radiology. The discoveries at the beginning of the century by Rutherford, Planck, Bohr, and Einstein corollated some of the enigmas concerning the relationship between the structure of matter and radiant energy. The fruits of further investigation were revealed during the early 1930's, when great discoveries were forthcoming. Chadwick discovered the neutron, Irene Curie and F. Joliot observed artificial radioactivity, Urey discovered heavy hydrogen, and Anderson described the positron. Shortly thereafter Fermi, Hahn, Strassmann, and others elaborated their observations on uranium fission. Perhaps the simple announcement by Strassmann and Hahn concerning their observations on nuclear fission might be termed the turning point in the development of the atomic bomb. The invention of the cyclotron by Lawrence permitted a means of artificially making radioactive isotopes, which made available such isotopes as radioactive iodine, radioactive phosphorus, and others for biologic investigation both as a means of studying metabolism by tagged ions and also as a means of treating cancer. Thus, shortly after the production of radioactive phosphorus, John Lawrence used these isotopes in the treatment of leukemia.

The success attendant upon the use of roentgen rays, and beta and gamma rays obtained from naturally occurring radium prompted the study of the effect of other beams upon cancer. Although the first neutrons were produced by Bothe and Becker at the University of Giessen in 1930, and were identified as neutrons a few years later by Chadwick, the invention of the cyclotron made available beams of fast neutrons which were collimated for clinical use by Aebersold. In 1937, Ernest Lawrence published *The Biologic Action of Neutron Rays;* as the beam was too caustic and produced too severe a tissue reaction, its use as a means of treating cancer was discontinued.

A modification of the use of the neutron beam for the treatment of cancer is now being investigated (1954) by Lee Farr and his associates at Brookhaven National Laboratories for the treatment of glioma. These investigators inject boron intravenously, and after a given period they bombard the site of the tumor with slowed neutrons by inducing a physical reaction in the boron to render it radioactive. The results to date are encouraging.

Fast proton and fast deuteron beams have also been employed as a means of treating cancer, but again the results are equivocal and they are now being investigated. Fast protons were described by Robert Wilson in *Radiology*, 1946.

Tobias, Anger, and Lawrence, in 1952, published their observations on the effects of the use of high energy deuterons and alpha particles generated at the 184 inch cyclotron in California. The nature of the beam was established, the rate of energy loss computed, and the biologic effects in comparison to those of 200 kv. roentgen rays were determined. Animal experiments have been computed and the authors stated that the possible application to radiotherapy is promising.

The use of artificially produced isotopes for corporeal distribution has been somewhat disappointing. Radioactive phosphorus has been utilized for the treatment of leukemia and polycythemia vera with success. Attempts to localize P^{32} in space-occupying tumors have been somewhat disappointing. Use of radioactive iodine has been successful in treating a few thyroid cancers which have an avidity for iodine. The isotopes, however, are of great use in studying the various metabolic reactions and in investigating the manner in which these reactions differ in the cancer patient and the normal individual.

The use of radioactive isotopes for teletherapy has been more successful. Cobalt 60 has been used extensively as a means for teletherapy. In 1952, a Teletherapy Evaluation Board was established with 20 medical schools and the Medical Division of Oak Ridge Institute of Nuclear Studies, which started a long term program to "investigate, develop, and evaluate radioisotopes for teletherapy." The following isotopes are being investigated: europium 152, cesium 137, and cobalt 60. A prototype unit has been constructed which can use any of the three isotopes interchangeably.

THE SURGICAL TREATMENT OF CANCER

The surgical treatment of cancer is the most effective method of curing this disease. The cancer surgeon, recognizing the limits of his science, is ever attempting to develop more effective methods of treating cancer. Surgical removal of cancer is the oldest method of treating this disease, reference to this fact being made in the most ancient medical writings. Celsus, in the first century A.D., advocated diagnosis by exploration and treatment by removal. Galen, in the second century, advocated thorough resection of malignant growths. DeMondeville, in the fourteenth century, advocated the excision of cancer "down to the roots." These broad general principles expressed by the earliest medical writers have been developed through the centuries so that in the middle of the twentieth century a more precise understanding exists pertaining to what is meant by "the roots" and as to how an adequate resection may be accomplished.

This has been effected by varied scientific advancements. Surgery as a polyphasic science benefits from contributions apparently distantly removed from the science of dissection. Thus the discovery of positive pressure anesthesia permitted intrathoracic manipulation; the discovery of insulin by Banting and Best (1922) permitted surgical extirpation of the pancreas; and the identification and synthesis of cortisone permitted adrenal resection. At the turn of the century surgical developments were relatively few. Abdominal surgery could not develop because of the high mortality rate from infection.

Peritonitis was a frequent complication. Lister's (1827–1912) work on antisepsis and asepsis laid the cornerstone for future advances. Von Bergmann and Schemmelbusch in Berlin developed the steam pressure sterilizer at the end of the nineteenth century. Halsted first used rubber gloves at the end of the century, and in 1900 William Hunter of Charring Cross Hospital, London, introduced gauze masks, thus completing the equipment of asepsis.

The remarkable progress of the ancillary surgical sciences now affords the surgeon great leeway in the scope of his operative efforts. The establishment of the diagnosis by biopsy and the development of certain chemical tests indicative of some cancers (Bence-Jones proteins in myeloma in 1848; chorionic gonadotropin in testicular tumors—Zondek, 1930; acid phosphatase in advanced prostatic cancer—Gutman and Gutman in 1938; and a few others) have given the surgeon the indication for surgical attack and the license for boldness and radicalness in attempting to extirpate the primary cancer and its satellites. On the other hand, he also has chemical data which contraindicate radical attempts at surgical extirpation.

Knowledge concerning the natural history of cancer and its modes of spread has permitted the intelligent planning of operative procedures to encompass in continuity the primary cancer and those echelons of spread technically resectable. The knowledge that certain tumors (e.g., rhabdosarcomas) spread by direct extension necessitates resection of the entire organ (entire muscle). The spread by implantation manifested by certain

cancers (ovarian cancer, pancreatic cancer) demands the most delicate gentleness during their resection to avoid spillage.

The spread by way of the lymphatics represents a major challenge to the cancer surgeon, and inclusion of the lymphatics in cancer operations represents one of the greatest surgical efforts at curing cancer. The great anatomists of the latter part of the nineteenth century and the first half of the twentieth century, such as Rouviere and Cuneo who have painstakingly demonstrated the courses of lymphatic drainage from various organs, have offered routes for the planning of cancer operations, which accomplishment represents one of the greatest surgical advances of this century. The abdominoperineal rectal resection (Miles), the radical hysterectomy (Wertheim), and the radical mastectomy (Halsted) are a few examples of cancer operations aimed at removing lymphatic metastases in continuity with the primary tumor, the so-called monobloc operation. The surgery of cancer might aptly be termed "the surgery of the lymphatics."

Cancer spread by way of the perineurial lymphatics produces symptoms and signs which often contraindicate surgical intervention. Some examples of these include severe pain from pancreatic cancer, vagal involvement by esophageal cancer, and invasion of the recurrent laryngeal nerve by bronchogenic cancer.

The common tendency of venous metastases frequently dooms surgical efforts to failure. The vertebral vein plexus described by Batson in 1940 has explained the bizarre phenomenon of cerebral metastasis from abdominal cancer without the production of intrathoracic deposits. Surgical efforts to control this form of spread consist of primary ligation of the blood vessels to certain tumors to prevent the development of blood stream emboli during the operation (ligation of the renal vessels during nephrectomy for Wilms' tumor) and resection of solitary metastasis to the lung or brain from distantly controlled primary tumors (fibrosarcoma, kidney and thyroid tumors). The extensive recent study by Willis on spread of tumors in the human body (1952) summarizes this subject. The behavior of certain tumors as regards their propensity and routes of spread determines the operability and extent of operation as well as focuses attention on the possibility of distant spread and if the latter has occurred the patient can be spared the rigors of a radical, extirpating operation.

Physiologic Aspects of Cancer Surgery

The great strides in the anatomic phases of surgery have focused upon the need for synchronization of the physiologic component of extirpative surgery into cancer operations. The radicalness of the attack, the increased morbidity, and the necessity of operation upon patients in the older age brackets, who are frequently poor operative risks, have necessitated an understanding of the metabolic alterations in the surgical patient. Every medical advance has been utilized to prepare the patient for the surgical experience. Thus, patients with pernicious anemia, diabetes, heart disease, and any host of metabolic disturbances can be made safe candidates for surgery. The observation by O'Shaughnessy (1831) and Schmidt (1850) of blood electrolyte abnormalities during cholera paved the way for application of the science of electrolytes to the treatment of the surgical patient. Coller and his group at the University of Michigan contributed greatly to this phase of surgical physiology, with emphasis upon the anionic changes. The recent development of the flame photometer and its early application to clinical surgery by Charles Fox (1951) has contributed knowledge of cationic abnormalities which have been studied extensively by Moore of Harvard and Moyer and his group.

The study of protein metabolism by Cannon of Chicago, and Whipple and his group in Rochester, New York, during the past 25 years has stressed this phase of physiology in the surgical patient. Studies of protein balance and the intravenous administration of amino acids, developed by Elman, have afforded a means of parenterally maintaining a positive protein balance in the surgical patient. Studies of altered anatomic and physiologic integrity due to gastrointestinal obstruction, and the development of intubation decompression by Wangensteen represent a milestone in the treatment of gastrointestinal cancer.

The history of blood transfusion of the surgical patient is indeed a fascinating developmental story, including many mystic beliefs as well as scientific facts. Transfusions could not be given safely in 1900 despite extensive efforts toward administering blood to patients during the preceding centuries, which started with the discovery of the circulation by Harvey in 1616 and which persuaded Christopher Wren in 1656 to inject medicants into the veins of dogs. The first successful animal transfusion was performed by Lower in

1665. In 1667 Denis administered blood from a lamb to a patient, but with the death of his patient transfusions were prohibited by an act of Parliament and later by a papal bull. Not until 1829, when Blundell in London described a successful human transfusion, was there any stimulus toward the investigation of the nature of human blood. The phenomenon of agglutination was observed, especially when human blood was mixed with that of other species. In 1901, Karl Landsteiner discovered the isoagglutinins of human blood, for which he was awarded the Nobel Prize. In 1908, Ottenberg developed methods for making blood typing practicable. The technique of tranfusion was still most difficult, and early attempts required the suture anastomosis of Carrel, developed in 1902, which was supplemented by another direct transfusion method developed by Crile (1907). All of these methods necessitated the sacrifice of the donor's artery. The development of a syringe technique of direct transfusion by Lindeman in 1913 was a great improvement. In 1914, the use of citrate by Hustin of Belgium permitted indirect transfusions, and its possibilities were extensively developed by Lewisohn of Mt. Sinai Hospital, New York. The recent developments of minor agglutinins and the Rh factor by Wiener, blood banks, and lyophilization and separation of certain constituents of the blood represent the recent contributions to blood administration so necessary for today's cancer surgery.

The great advances which have been made in a relatively short period can be appreciated from a quotation made by a famous surgeon just 82 years ago. In 1873, Sir John Erichsen, Professor of Clinical Surgery at the University College Hospital, London, and for whom Lister had worked as House Surgeon, defined those portions of the human body which would forever remain sacred. He stated, "The abdomen, chest, and the brain will be forever shut from the intrusion of wise and humane surgeons." While exposed regions (face, extremities, breasts) were operated upon many centuries ago, the surgery of visceral cancer developed in a definite time sequence. First, the abdominal and genitourinary systems, then the central nervous system, and, lastly, the chest, were invaded by the surgical scientists.

CANCER OF THE HEAD AND NECK

Many operations performed today in the treatment of cancer of the head and neck were described by surgeons during the seventeenth, eighteenth, and nineteenth centuries. These operative procedures, well conceived and executed, gained little popularity because the surgical treatment of many cancers, especially cancer of the head and neck, was harnessed by the high mortality which accompanied each of the surgical attempts. For example, in 1880, Gluck reported upon the hazards of performing a pharyngolaryngectomy and described the situation prevalent at that time as follows: "A normal course surely was seldom seen by the older authors; erysipelas, phlegm, secondary hemorrhage, mediastinitis, bronchitis and septic bronchopneumonia, sepsis acutissima, shock, particularly delirium cordis, and insufficienta cordis with consecutive paralysis of the heart carried off the patients, so that a mortality of 25 per cent after these severe operations was really at the time too low a figure statistically."

In 1884, General Grant's physicians suggested the technical practicality of performing a combined glossectomy and radical neck dissection, and from their report in the Medical Record of March 21, 1885, the following is stated.

"During the past week, the local disease of General Grant has shown no more tendency toward progressive ulceration. Dr. J. H. Douglas, Henry B. Sands, and George F. Shradie, who were present, made a thorough examination of the General's throat with a view to discussing the expediency of a radical operation for the removal of the growth. Such a measure would involve the division of the lower jaw in the median line, the extirpation of the entire tongue and the greater part of the soft palate, together with the removal of the ulcerated and infiltrated fauces, and the indurated glandular structures under the right angle of the lower jaw. This was considered mechanically possible despite the close proximity and probable involvement of the tissues adjoining the large arteries and veins in the neighborhood of the ulcerations. In the best interests of the distinguished patient, the surgeons did not feel inclined to recommend the procedure."

The high incidence of infection following surgery about the head and neck discouraged all surgeons of that time from the hope of a primary union. Le Bec, Crile, and New devised two stage operations in order to permit the patient to "vaccinate" himself against infection at the time of removal of the larynx. As recently as 1937

Portmann devised a two-stage operation, leaving a pharyngostomy to be closed at a later date.

Crile, who was one of the great pioneers in cancer surgery, reported a mortality of 13 per cent for radical operations about the head and neck at the turn of the century. He was one of the first to attempt a combined operation, removing a primary tumor of the intraoral region in continuity with the cervical lymph nodes, but because of the prohibitive mortality, he finally limited this operation to tumors of the floor of the mouth and gums. In his report in 1906 he described such apprehensions.

It is thus possible to trace the surgical development in treating cancer of the head and neck from simple excision of the neoplasm, through attempts to obtain better exposure for such local excisions, to the realization of the necessity of resecting metastases to the lymph nodes if cures were to be accomplished. The progressive resections from the localized neoplasm to composite resections have removed practically all anatomic barriers. Emphasis is now being directed to the application of sound surgical judgment before the performance of such radical mutilating operations.

The decade commencing with 1930 ushered in the era of safe surgical resection of head and neck cancer. The discovery of antibiotics, intravenous pentothal anesthesia, blood banks, the development of dermatomes for skin grafting, and improved reconstructive procedures inaugurated the era of radical extirpative surgery.

Tongue Cancer

Cancer of the tongue was one of the first cancers to be attacked surgically. Because of the association of the tongue with the medium of expression it had been considered in olden times as a benefaction from the Almighty. Accordingly, any affliction of the tongue was deemed divine punishment, especially for such crimes as heresy and blasphemy. The punishment was usually exeresis of the tongue. This barbaric torture demonstrated that glossectomy could be tolerated, hemorrhage was not too severe and could be controlled, and speech even continued after apparent total glossectomy.

A history of the treatment of tongue cancer through the nineteenth century was related in 1885 by Henry Butlin, surgeon to St. Bartholomew's Hospital in London. The preliminary statements about the pre-twentieth century methods of treating lingual cancer have been obtained largely from Butlin's monograph. As early as 1658, Pimpernelle successfully excised lesions of the tongue. One year later, Marchetti resected a portion of the tongue by actual cautery, and Ruysch excised a portion of the tongue with the scalpel and cauterized the base with a hot iron. About 100 years later, Guthrie, in England, first excised a cancer of the tongue with a knife and then cauterized the cut surface. In the early 1800's, ligation became popular. Thus, Inglis ligated a tongue lesion by drawing cords through the tongue and around the tumor. Major placed a ligature about the tumor by splitting the organ down the center, and Cloquet, in the same year (1827), split the organ and introduced a ligature through a suprahyoid incision and strangled the diseased half of the tongue. The first wedge excision for tumor of the tongue was performed by Langenbeck in 1819, and Mirault preliminarily ligated the lingual artery. During the latter half of the nineteenth century, tumors were removed essentially by écrasement, either mechanically as performed by Chaissaignac, or galvanically as performed by Middeldorpf.

Further attempts to achieve adequate excision of the tongue by improved exposure were made during the latter half of the nineteenth century. Jaeger (1831) first divided the cheek to gain access to the tongue, and Maisonneuve (1858) divided both cheeks. Further attempts at exposure were made by division of the lower jaw. Roux (1836) divided the lower jaw and the lip in the midline. Billroth (1862) divided the jaw and soft parts at the side in two places and turned down the flap of skin and bone so formed, replacing and wiring the bone afterward. Von Langenbeck (1875) divided the jaw and soft parts opposite the first molar tooth on one side to gain access to the base of the tongue and removed part of the tongue as well as the adjacent lymph nodes.

In 1838, Regnoli opened the floor of the mouth from below by an incision from the middle of the hyoid bone to the chin. In 1871 Billroth modified this incision by extending both ends of the curved incision farther back. Kocher, in 1880, introduced a method of opening the mouth from behind and below the angle of the jaw to reach the base of the tongue and remove it with all the accessible lymph nodes. Butlin, during the end of the last century and the early

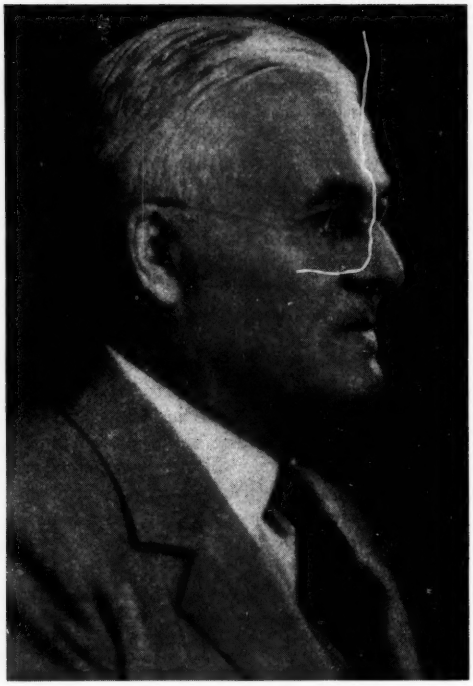


FIG. 13. George W. Crile.

part of this one, performed many modifications of glossectomy for cancer.

The operations as performed today consist essentially of four procedures. The wedge excision for relatively benign tongue tumors is the same procedure as that described by Langenbeck in 1819. Hemiglossectomy for local tumors is essentially the same as the procedure described by Whitehead. The operation of resecting the tongue and floor of the mouth combined with neck dissection is essentially a modification of the procedure described by Kocher in 1880. In order to assure an en bloc resection, the mandible was incorporated in the resection; this operation was first performed by Grant Ward of Baltimore in 1932. Martin, of Memorial Hospital in New York, has reported on its use in hundreds of patients with a negligible mortality.

In an effort to prevent mutilation from resection of the mandible, operations are being performed in a manner which spares the mandible. Robben, of Grant Ward's Clinic, confirmed Polya's observation, made in 1902, that the lymphatic drainage penetrates the periosteum in about 50 per cent of the cases and does not infiltrate the mandible. Kremen (1951) described a procedure in which the mandible is split in the midportion, the intraoral contents are swung into the neck wound, and a radical neck dissection is performed in continuity with the intraoral contents; the mandible is then wired back into position by a modification of the operation originally described by Billroth in 1862. The composite operation, described both by Ward and by Slaughter, in which a neck dissection is first performed, after which an inframandibular incision is made and the intraoral contents are brought down through this incision, is a modification of Regnoli's procedures (1838).

Coincident with the development of the surgical attack upon tongue cancer was the development of methods of radiotherapy to control this disease. Martin, of New York, designed intraoral cones for attachment to x-ray sources and used them in the treatment of tongue cancers. External ports for the administration of roentgen therapy were in common use during the past few decades. The use of radium interstitially and in molds was described in detail by Sir Stanford Cade. Constance Wood of England has accomplished extraordinary end results by the scientific application of teleradium.

The Development of Neck Dissection for Cancer

Credit for the development of radical neck dissection as performed today belongs to the late George Crile, who in 1906 reported a series of such operations. The significant difference in the concept of neck dissection as developed by Crile is that previously the operator dissected down upon the nodes in order to enucleate them whereas Crile advocated the development of skin flaps and performed the dissection to encompass all the cervical lymph nodes en masse. The operation as described and practiced by Crile at the turn of the century is essentially the same as performed today, namely, resection of the jugular vein, the sternocleidomastoid muscle, and of all of the areolar and lymphoid tissues of the neck triangles. He advised temporary occlusion of the common carotid artery to effect hemostasis, and was aware of the permanent damage which would develop from cerebral anoxia. He even practiced resection of the floor of the mouth in continuity with the neck dissection.

Many earlier surgeons had attempted partial or incomplete dissection of metastatic cancer in

EXCISION OF CANCER OF THE HEAD AND NECK.

WITH SPECIAL REFERENCE TO THE PLAN OF DISSECTION BASED ON ONE HUNDRED AND THIRTY-TWO OPERATIONS.*

GEORGE CRILE, M.D.
CLEVELAND, O.

Though signal advances have been made recently in many surgical problems, the treatment of cancer of the head and neck has, it would seem, neither received the attention nor kept the pace of progress in other fields. These unhappy cases are too often regarded as specters at the clinic. The operative treatment is hampered by tradition and conventionality, and the tragic ending of so large a proportion of these cases has held back lay and even professional confidence.

In this paper it is intended to present an outline sketch of the conclusions regarding the surgical treat-

* Read in the Section on Surgery and Anatomy of the American Medical Association, at the Fifty-seventh Annual Session, June, 1906.

FIG. 14. First portion of the article in which Crile described the radical neck dissection; first published in *J. Am. M. Ass.*, 1906, 47: 1780.

the cervical lymph nodes. Chelius, in 1847, observed the involvement of lymph nodes by cancer metastasis from the oral cavity, but considered this complication indicative of incurability. The operation described by Kocher in 1880 required a dissection of the submaxillary triangle through a superjacent incision and thence

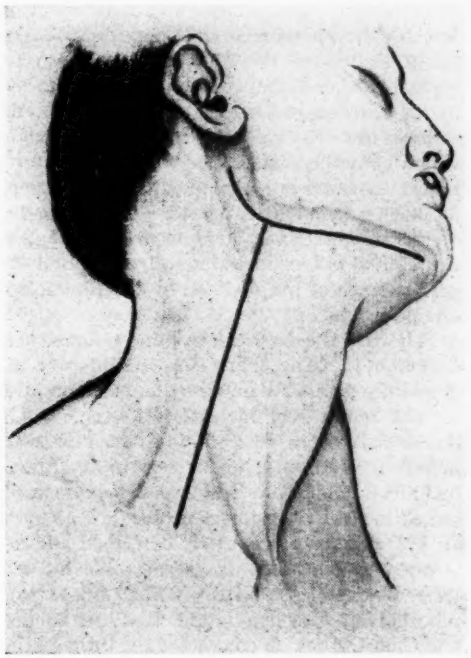
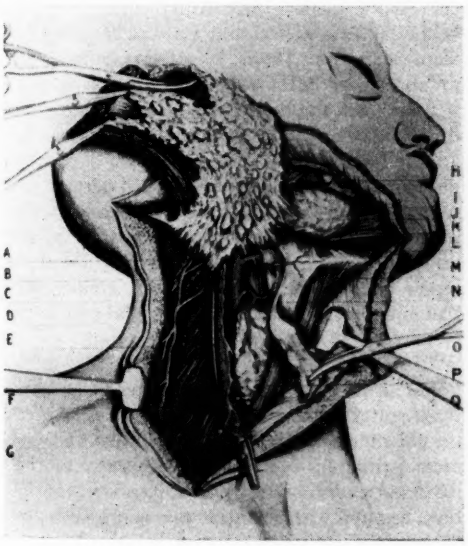


FIG. 15. Incision utilized by Crile in performing neck dissection, from his original article.



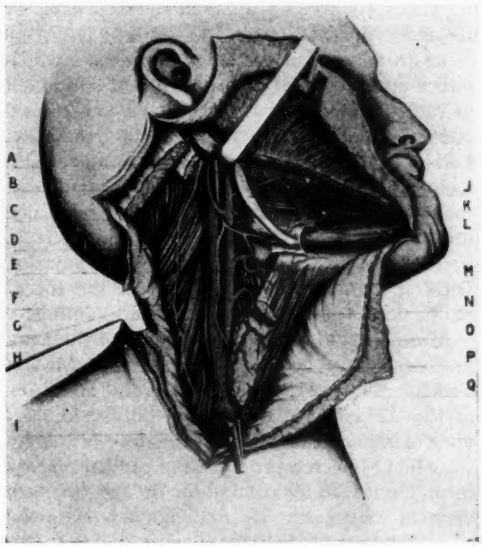


FIG. 16. Illustrations demonstrating the scope of the neck dissection as originally described by Crile.

to the tongue, with excision in continuity of the lingual cancer and the cervical metastases. Kocher further extended the operation to design the typical Kocher Y-shaped incision. Boyd, in 1887, in his revision of Druitt's *Modern Surgery*, described the removal of cervical lymph nodes which contained metastatic cancer, and stated that it was necessary to expose the carotid artery, jugular vein, and vagus nerves. Butlin performed segmental resections of cervical lymph nodes through a trocar incision and advocated the performance of prophylactic neck dissection in certain instances.

Following the description of the complete neck dissection by Crile, many surgeons adopted this procedure and it became the standard operation for the removal of metastases to the cervical lymph nodes. This operation has been extended in recent years and, under certain conditions, includes a bilateral radical neck dissection at the same time that the primary neoplasm is resected. In 1927, Semken accurately described and advocated radical neck dissection while the majority of oncologists in the United States were preoccupied with irradiation. In 1931, Spencer and Cade of London completed the third edition of "Diseases of the Tongue" to follow Butlin and Spencer's 1900 second edition. They clarified the criteria for the lateral neck dissection and advised that recurrent metastatic cancer in the neck be either reoperated upon in selected cases or treated by irradiation.

In an analysis of the balance of forces which either stimulated or retarded the development of radical surgery in the oral cavity and neck, one must consider the impact that irradiation had on the treatment of malignant tumors in this location. Enthusiasm for irradiation in the treatment of these malignant tumors was sustained until approximately 1940, by which time certain undesirable late effects of intensive irradiation became manifest. Re-evaluation of the therapeutic values of irradiation was disappointing.

Monographs dealing with cancer of the head and neck have been written by Blair, Moore, and Byars in 1941, and by Ward and Hendrick in 1950. Hayes Martin in 1951 published a review of 1,450 cases of neck dissection; in this review he has been a proponent of radical surgery in preference to irradiation for the treatment of cervical metastases. He does not advocate the so-called "prophylactic" or elective neck dissection.

The technique of Conley, whereby a resected portion of the internal or common carotid artery is replaced by a vascular graft to prevent hemiplegia and death, is at times a life-saving measure. Martin's experience with 87 consecutive common and/or internal carotid artery ligations between 1926 and 1951 was attended by an overall mortality of 31 per cent, although in the last 34 cases (1948–1952) the mortality had diminished to 12 per cent, an improvement which he attributes to the fact that the blood pressure was maintained throughout the entire operation, especially at the time when the ligation was performed (1953).

Cancer of the Lip

The three most important factors permitting adequate control of labial cancer are (1) control of infection, (2) knowledge of the lymphatics of the lip, and (3) the development of plastic surgical repairs to effect a reconstruction and avoid a "leaking" mouth. The description of the lymphatic system of the lips was first accurately recorded by Most in 1906. Additional reviews by Sassier in 1927 and Rouviere in 1938 furnished an anatomical basis for studying the routes of dissemination of lip cancer.

At the end of the last century, in 1877, Estlander had described a rotated triangular flap to repair the lip defect after excision of the cancer. At the turn of the century various methods of cheiloplasty with sliding full-thickness lip flaps were devised by Davis, Ivy, Denonvilliers, Szymonowski, and others.

Based on the knowledge of the lymphatic drainage of lip cancer, a common plan has been adopted of resecting the primary lip cancer and performing a bilateral suprahyoid cervical dissection. Low voltage x-rays applied with light filtration, at relatively short target-skin distances and in fractionated series, or radium employed topically or interstitially has been equally effective in the treatment of superficial labial cancers.

Cancer of the Buccal Mucosa

Polya, in 1926, described a variety of operations suitable for extirpation of cancers of the buccal mucosa. Richards has contributed technical principles for radiation therapy of these cancers. Radon seeds and radium needles have been applied with scientific precision, with doses determined by biophysical principles and protective shields to conserve normal intraoral tis-

sues; the results of such radiation therapy are comparable with those obtained by surgical excision.

Tumors of the Jaws

The adamantinoma, first described by Malassez in 1885, is usually benign, but metastases have been described by Thoma, and by Byars and Sarnat in 1945. Many of the prostheses were developed originally by Kazanjian at the completion of the first world war. The extensive studies of Thoma on the pathology of oral tumors have contributed greatly to an understanding of the pathology of these complex tumors of dental origin and have led to methods for their eradication.

Salivary Gland Tumors

Clementz in 1882, Collet in 1895, and Curtis and Phocas in 1899 contributed to our knowledge of the natural history and pathology of these interesting neoplasms.

McFarland, in 1926, described the natural history of these tumors and commented on their incidence and the choice of therapy. His assertion that they should be permitted to ripen before excision was an unfortunate influence which persisted for many years. Improved classifications of these neoplasms based on a better knowledge of their histogenesis were given by Stein and Geschickter in 1934, Marshall and Miles in 1947, Rawson and his associates in 1950, and Kirklin and his coworkers in 1951. The monograph by Ahlbom in 1935 gave a valuable review of the clinical behavior of tumors of the salivary gland and emphasized the techniques and results of radiotherapy. Such surgeons as Bailey (1947) and State (1949), Hendrick, Ward, and Lacy (1951), Klopp and Winship in 1950, Martin (1952), and, most recently, Frazell have independently arrived at plans for surgical excision which afford reasonable prospect of cure. Blady and Hocker in 1939 advanced sialography as an aid in the differential diagnosis of lesions of the parotid gland.

Malignant tumors of the parotid gland treated by radical parotidectomy often require sacrifice of the facial nerve. Repair following resection of the facial nerve has been devised by Brown and others by the use of fascial slings extending from the temporal muscle down to the eye, lip, and chin. Attempts at neurorrhaphy after severance of the facial nerve by transplantation of the twelfth cranial nerve or the hypoglossal nerve have for the most part not been too successful. The recent nerve grafting developed by Conley, in which he uses the great auricular nerve as a homograft, has proved successful.

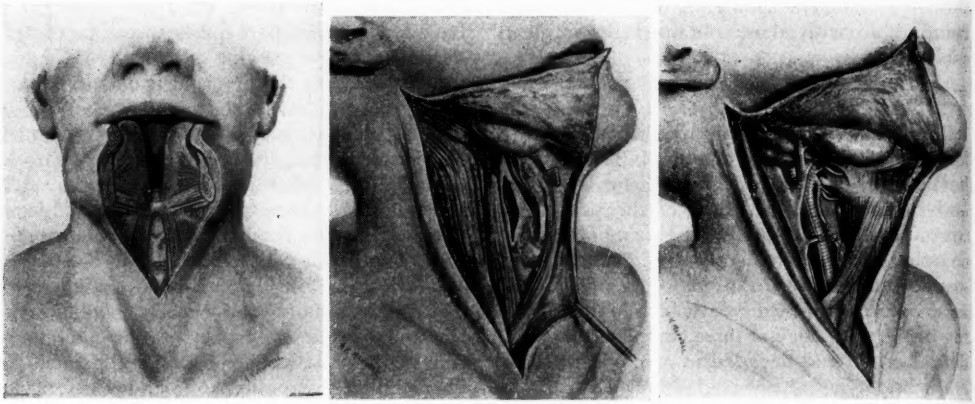
Thus, the first half of the twentieth century has permitted a nosologic classification of parotid tumors, has dispelled the misconception that these tumors frequently originate from multicentric foci, and has resulted in an acceptance of a radical operation which is curative in most cases. Radiation therapy has not been too effective. Total parotidectomy for cancers involving the retromandibular projection of the gland may require the removal of a portion of the mandible for complete extirpation. The knowledge of the incidence and routes of lymphatic metastasis has resulted in operations devised for conjoined resection in continuity of the primary parotid cancer and the ipsilateral cervical lymph nodes.

Cancer of the Paranasal Sinus

In 1870, Sir William Fergusson devised his famous incision for access to the antrum, and in 1901 Alexander Hugh Ferguson further described the technique of radical antrectomy. The reflection of the cheek flaps after the incision along the philtrum and nasolabial fold permits resection of the superior maxilla, or it offers exposure for the application of radium implants. MacFee (1935) reported upon the successful employment of this operation with refinements, described by Ward and himself: the use of fascial slings in the infraorbital plate to prevent eye drop, free skin grafts to cover denuded regions, and the prosthesis developed by Kazanjian, Ackerman, and others to fill in defects of the palate corrected the operative complications.

Cancer of the Pharynx

Pharyngeal cancers have routinely been treated by irradiation. It was for this group of tumors that Regaud and Coutard developed the fractional method of irradiating cancer, which has since become classic. However, the results have not been satisfactory and salvage rates of more than 10 per cent are seldom obtained. In 1948, Harold Wookey of Toronto originated a surgical procedure for removal of the hypopharynx, esophagus, trachea, and larynx (if necessary) for cancer of the hypopharynx and base of the tongue, and, by means of an ingenious utilization of the adjacent skin, constructed a skin tube to replace



a b c

FIG. 17. Pharyngotomy as described by Trotter. a, shows anterior translingual pharyngotomy, with exposure stage completed. b, Lateral pharyngotomy, early stage. c, Lateral pharyngotomy, with exposure stage completed. The gland dissection has been done, and the resulting cavity is secluded by suture of the sternomastoid and digastric posterior belly to the prevertebral muscles.

the missing segment of the pharynx. This operation is an improved modification of an operation described by Trotter in 1926. More recent use of a free skin tube or of some prosthetic device to replace the missing segment of pharynx and esophagus has been developed. These methods include the use of nonirritating plastic materials (polyethylene, nylon), inert metals such as vitallium or tantalum, or the use of these elements as a stent to prevent contracture of a skin tube which is formed about the stent. The refinement of these techniques and their proper application are now being adjudged (Conley, Kremen, Edgerton, and Cade).

Cancer of the Nasopharynx

Prior to the twentieth century few references were found pertaining to nasopharyngeal cancer. Jackson, in 901, discovered only 13 cases in the world literature, of which the earliest case report appeared in 1837. Not until 1921 did an accurate description of this cancer appear. Regaud and Reverchon, and Schmincke independently published articles describing the pathologic features. Trotter, in 1911, had described the classical Trotter's triad resulting from nasopharyngeal neoplasms, viz., impaired hearing, neuralgia of the second branch of the trigeminal nerve, and asymmetry of the soft palate.

Since 1921 comprehensive reports have been published by New (1922, 1925, 1931, and 1943), Furstenberg (1938), and C. Martin (1939). Blady (1938) described a nasopharyngeal radium applicator to supplement external irradiation. Because of the radiosensitivity of these neoplasms, excellent palliation but few absolute cures are obtained. Schmincke described a specific tumor containing many lymphoid elements in addition to the carcinomatous elements, which has since been called "Schmincke tumor" or lymphoepithelioma. The identification of the juvenile nasopharyngeal angiofibroma occurring in adolescent boys and the devascularization of the tumor with testosterone therapy have permitted surgical and radiation treatment to be successful and prevent the sometimes fatal complications of sepsis and hemorrhage. With such induced maturation of the boy, this particular tumor tends to undergo spontaneous involution.

Cancer of the Larynx

During the past 50 years laryngeal cancers have come to be considered as of two major clinicopathologic types which are of different localizations, i.e., intrinsic and extrinsic (Krishaber, 1879). Whereas tumors of the intrinsic larynx (vocal cords) are usually slow-growing, present a relatively low degree of malignancy, metastasize late because of the dearth of lymphatics in the cords, and are readily cured in the early stages by either surgical extirpation or irradiation, the neoplasms of the pharynx and "extrinsic

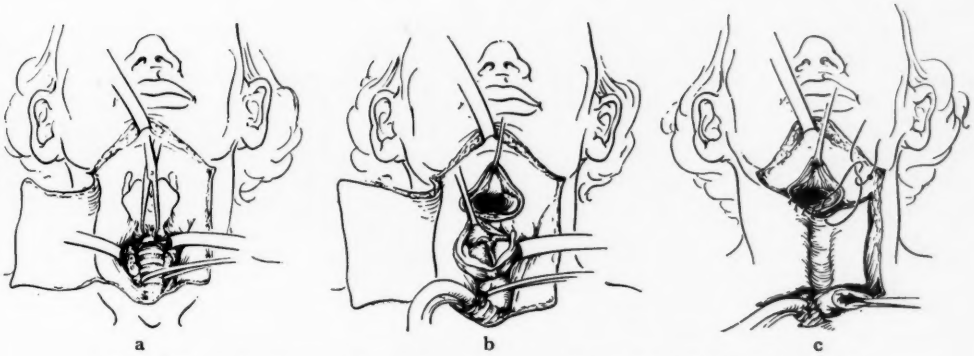


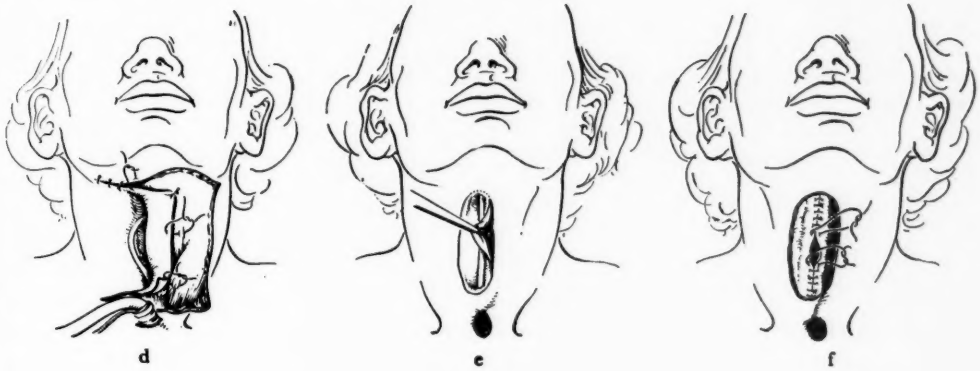
FIG. 18. Successive stages of pharyngolaryngectomy as described by Wookey (a through f).

larynx" are more anaplastic, evoke a vascular and lymphoid response, metastasize relatively early because of the abundant lymphatic supply, and are radiosensitive but not particularly radiocurable. The surgical attack upon these neoplasms which is now being carried out necessitates critical evaluation to adjudge if radical attempts at extirpation are justifiable.

Manuel Garcia of Vienna, a professional singer who wished to watch his vocal cords in action, devised a reflecting mirror in 1855. This inaugurated the science of laryngology and permitted the clinical detection of laryngeal cancer. Turck and Czermack in Vienna became enthusiastic about laryngoscopic examinations and Vienna thereby became the center of laryngology for the rest of the nineteenth century. Aretaeus, in 100 A.D., referred to laryngeal cancer, and Galen in 200 A.D. described malignant ulceration which exhibited infiltrating characteristics and led to dyspnea by compression of the upper airway. Morgagni, in 1732, clearly described cancer of the larynx. In 1846, Trousseau performed the first tracheostomy for the relief of phthisis due to laryngeal carcinoma, and in 1851 Gurdon Buck, in America, without benefit of anesthesia, performed the first laryngofissure for removal of an intrinsic cancer. MacKenty declared that not until 1876 was one cure reported, the ultimate gain of 12 laryngectomies. From 1876 to 1886, 108 laryngectomies resulted in 21 cures, and from 1886 to 1901, 186 laryngectomies resulted in 69 cures.

Previous to 1900 efforts were made to treat laryngeal cancer by intralaryngeal extirpation. Reports of cures of extensive cancers existed. MacKenty had emphasized the fact that this procedure is not indicated for treatment, only for a biopsy. Chiari stressed the necessity for early operation as soon as the biopsy had been taken.

Thyrotomy or laryngofissure. This operation was first described by Brauers in 1833 for the



treatment of polyps and was adapted by Ehrmann in 1844 for cancer. The first reported thyrotomy is attributed to Gurdon Buck, but his patient died of recurrent cancer 10 months later. Solis Cohen repeated the operation in 1868 with a resultant cure. Bruns, in 1878, collected 19 thyrotomies with recurrence in all of the cases but one. In 1881, Foulis and Czerny contended that cancer of the larynx could be cured only by total laryngectomy. Butlin concurred, but certain proponents of laryngofissure persisted in performing this operation and it gained marked favor during the end of the last century. Thus, Chiari reported 41 thyrotomies with only 3 operative deaths, 11 recurrences, and 15 cures. Butlin, in 1908, reported 41 operations on 37 patients, 31 of whom were subjected to thyrotomies. There were 5 operative deaths and 15 patients were living after 3 years. He regrets his conversion to thyrotomy in this article and stated that if he had performed a total laryngectomy he would have saved several of the patients who died from recurrences. St. Clair Thomson, in 1922, reported 51 thyrotomies with 2 fatalities; 30 of the 49 patients were alive and 3 recurrences had developed at periods varying from 1 to 13 years. Jackson, in 1922, performed 45 thyrotomies with no surgical mortality but 20 per cent recurrence. MacKenty reported 8 laryngofissures and 12 "window resections" between 1906 and 1920 with a total of 15 recurrences. Regarding the status of thyrotomy for treating laryngeal cancer, MacKenty stated: "The keen observation and skill of these two Englishmen (Semon and Butlin) revived general interest in thyrotomy which, when its proper limitations were apprehended, began to give encouraging results. It became apparent that this operation was suitable only for incipient cases. The exact meaning of incipient must be left to the future for determination, since the controversy is still going forward though, I am glad to say, less acrimoniously than formerly. As experience accumulates, the sphere of thyrotomy contracts. It is on the fixation of its limitations that we are not yet all in accord."

Hemilaryngectomy. The first partial removal of the larynx was performed by Maas of Breslau in 1876. In 1878 Billroth removed part of the larynx and so popularized the operation that in 1907 Fred Sendziak was able to collect 224 cases from the literature. At this time Chiari reported 32 cases with recurrence in 15, in 1 as late as 6 years after operation. Prior to 1917 MacKenty performed 6 hemilaryngectomies with no fatalities, but a 75 per cent recurrence rate.

Total laryngectomy. The first total extirpation of the larynx was performed for syphilis by Watson of Edinburgh in 1866. From 1870 to 1873, Czerny was performing total laryngectomies on dogs, and when this procedure was demonstrated to be practical, Billroth, assisted by Czerny, performed the first laryngectomy for cancer on December 31, 1873. The patient survived the operation but died of recurrence 8 months later. Prior to 1907, Sendziak collected the statistics on about 500 total laryngectomies performed to that date. The danger of the operation was so great that Gluck in 1881 devised the two-stage operation, which was popularized and utilized generally during that era. At the beginning of the century reports by Butlin in 1908 and Gluck and Sverensen in 1912, and, later, reviews by Moure in 1921 and Lewis in 1923 all demonstrated the feasibility of total laryngectomy. Each worker added certain refinements in technique and demonstrated that laryngeal cancer can be cured by this procedure with relative safety to the patient. The development of the artificial larynx for speech after total laryngectomy by von Bergmann, MacKenty, and Tapia made the operation more bearable to the patient.

The extension of the surgical treatment of laryngeal cancer by en bloc laryngectomy with radical neck dissection (either unilateral or bilateral) and including pharyngeal and esophageal structures (now that methods have been developed to establish continuity of the digestive tract) affords improved hope for cures.

Treatment of laryngeal cancer by irradiation. At the turn of the century and up to the present date, laryngeal cancer has also been treated by various radiation modalities. Diagnosis by roentgenograms of the larynx as described by Coutard in 1922 and the use of tomograms developed by Leborgne in 1936 permitted appraisal of the extent of the laryngeal cancer. One of the earliest reports was that of Holt Diggle who, in 1937, reported a 22.2 per cent recurrence in his group of patients treated by radium. Henry Coutard, a proponent of irradiation of laryngeal cancer, developed the science to a high degree of efficiency with serial fractionated treatments through multiple ports. Recent reports of the effects of irradiation on laryngeal cancer are those of Lenz of New York and Cutler of Chica-

go, who demonstrated the ability of roentgen radiation to cure certain laryngeal cancers. Ackerman and Regato (1954), commenting on the irradiation of laryngeal cancer, stated that cure lies between the narrow limits of enough and excessive irradiation. The use of radium molds and interstitial needles has been abandoned for the most part, but telecurietherapy is utilized by Cade, Lederman, Wood, and others. Leroux-Robert of the Curie Institute, Paris, has combined surgical extirpation and irradiation of laryngeal cancer and contends that this method offers the patient the best chance for cure.

Cancer of the Thyroid

"Who would believe that there were mountaineers
Dew lapped like bulls,
Whose throats had hanging at them
Wallets of flesh; or that there were such men
Whose heads stood in their breast?"
The Tempest.—Shakespeare.

The tenets for treating cancer of the thyroid are products of the twentieth century. Goiter, a term used to designate any swelling of the neck and believed to have arisen from a corruption of the latin term *gutter* (throat) has been known since the Hindu writings of Atharba Beda before 1500 B.C. Chinese manuscripts in 1600 B.C. reported beneficial effects from eating seaweed or burned sponge. The treatment for goiter was developed on the basis of chance observation before anything was known concerning its origin or nature. The endemic distribution was described by Marco Polo in 1271, who found goiter in the people of Yarkand. Michael Angelo, while painting the Cistine Chapel, wrote, "I've grown a goitre while living in this den, as casts from stagnant streams in Lombardi, or in what other land they hap to be." In 1816, Prout, of England, demonstrated that iodine was the most effective treatment for goiter; this was just 4 years after the element iodine had been recognized by Gay-Lussac, having been discovered by the manufacturer of saltpeter, Courtois, in 1812, during the Napoleonic war.

In 1913, David Marine demonstrated that benign thyroid tumors contained less iodine than normal thyroid tissue and that the more embryonic the tumor structure, the less iodine in it. In 1916, Allen Graham determined the functional status of thyroid tumors by determining the capacity of such tumors to promote the maturation of tadpoles. He found a close correlation between the maturation principle and the iodine content of the tumor, and noted that one cancer did not contain either.

In 1923, Plummer found that iodine diminished the hypersecretion of hyperthyroidism, which led to the preoperative administration of iodine to patients subjected to thyroidectomy. In 1924, Marine discovered a relationship between hyperplasia of the thyroid due to iodine deficiency and the development of benign adenomas, and in 1928 Wegelin suggested that hyperplasia was a natural precursor to neoplasia. Bielschowsky (1944) observed that tumors developed in the thyroid glands of rats maintained on allyl-thiourea, and described the relationship between thyroid tumors and pituitary dysfunction.

Radioactive iodine^{131} provided a tool for studying thyroid physiology. Hertz, Roberts, and Evans first observed this relationship in 1938, and shortly thereafter Hamilton, Soley, and Eichorn employed audioradiographic techniques in demonstrating the localization of iodine in human thyroid tissues. Hamilton, Soley, Hertz, and Roberts in 1941 showed that radioactive iodine could be used to treat hyperthyroidism, and Frantz, Ball, Keston, and Palmer in 1944 found that a functional cancer of the thyroid would concentrate radioactive iodine. Leiter, Seidlin, Marinelli, and Bauman (1946) had a patient with functional metastatic cancer of the thyroid which was inhibited by thiouracil and other such agents. Rawson, Marinelli, Skanse, Trunnell, and Fluharty (1948) showed that total thyroidectomy induces function in metastatic tumors from the thyroid in a certain proportion of cases, and that the thyrotropic hormone stimulated the iodine-collecting capacity of some of these tumors, thereby providing a method for encouraging certain metastatic thyroid cancers to absorb radioactive iodine and thus be destroyed by its irradiation.

The classification of neoplasms arising from the thyroid gland and an understanding of the natural history of the various types, plus the recognition that certain tumors are very benign and slow-growing (papillary carcinoma) whereas others are highly malignant (giant cell carcinoma), provided criteria for the methods of treating the various types. These data have been summarized in the recent book by Thomas McGavack, entitled *The Thyroid.*

The surgical treatment of thyroid neoplasms. The performance of thyroidectomy is an operation

which can be performed with relative ease. More than 100 years ago the operation was deemed so dangerous that the French Academy (1850) prohibited operation for goiter. In a fascinating story by Halsted titled, *The Operative Story of Goitre*, published in the Johns Hopkins Bulletin in 1920, a dramatic account of the hazards of thyroid surgery is outlined. Halsted quotes Gross, who made the following comment in 1866: "If a surgeon should be so adventurous or foolhardy as to undertake the enterprise, I shall not envy him or his feelings while engaged in the performance of it or after he has accomplished it, should he be so fortunate as to do this. Every step he takes will be environed by a torrent of blood, and lucky will it be for him if his victim lives long enough for him to finish the horrid butchery. Should the patient survive the immediate effect of the operation, if this it may be called, death will almost be certain to overtake him from secondary hemorrhage, or from inflammation of the cervical vessels, esophagus, and respiratory organs. No honest and reputable surgeon, it seems to me, would ever engage in it."

Thyroid surgery had its inception at the end of the nineteenth century. Billroth, who had operated upon almost 50 patients between 1877 and 1881, with a mortality of 8.3 per cent, described postoperative tetany and recognized the danger of damage to the recurrent laryngeal nerve during the operation.

Kocher was the outstanding thyroid surgeon during the last half of the past century. Between 1889 and 1898 he performed more than 600 thyroidectomies with but 1 fatality. At the time of his death, in 1917, Kocher's clinic had reported on more than 5,000 thyroidectomies. Kocher first ligated the arteries, demonstrated the danger of indiscriminate iodine administration, performed clinical follow-ups on his patients, and advocated lobectomy, removing both lobes only for cancer. He advised that no attempt be made to separate adherent tissues in malignant goiter—"they must be cut around and removed en toto with the goitre." He also advised resection of the contiguous organs (trachea, esophagus) if they were invaded by cancer. Bloodgood (1905–06) had reached the conclusion that once cancer of the thyroid could be diagnosed clinically, there was little hope for the sufferer. He was thus one of the first to recommend the removal of apparently benign thyroid tumors to prevent the subsequent development of carcinoma.

At the turn of the century, the great American pioneers, Halsted, the Mayo brothers, and Crile, revised the operation of thyroidectomy. The Mayos always ligated the thyroid vessels primarily and instituted the multiple stage operation. Crile was most active in the study of shock and how to avoid it during the operative procedure. The reintroduction of iodine by Plummer in 1923, the discovery of the antithyroid drugs, and their application to medicine and surgery by Astwood in 1943 made thyroidectomy a relatively safe operative procedure.

An appreciation of the high incidence of metastases to the lymph nodes has resulted in the adoption of thyroidectomy in continuity with a radical neck dissection. The observation by Watson and Pool that cancer of the thyroid involved the opposite lobe in one-third of the cases has resulted in the performance of bilateral lobectomy or total thyroidectomy for more malignant forms of cancer. The observation by Oliver Cope concerning the early spread of thyroid cancer to the prelaryngeal nodes resulted in the appellation "the delphinian node," after the oracle at Delphi. The identification of tumor in the nodes offers a means of diagnosing a metastasis from a silent thyroid cancer. The discarding of the theory of aberrant thyroid tissue, notably by Pemberton of the Mayo Clinic, caused relabeling of the so-called lateral cervical thyroid deposits as metastases from either an overt or occult primary tumor of the thyroid. The accepted treatment for thyroid cancer today is a thyroidectomy with radical neck dissection.

Parathyroid Tumors

The discovery by Mandl, in 1926, of the relationship of parathyroid tumors to hyperparathyroidism led to the elucidation of the functions and pathologic physiology of the parathyroid glands. The discovery that certain bone cysts associated with other abnormalities of calcium metabolism are all the results of altered parathyroid metabolism represents one of the true dramas of modern surgical physiology. Either a functional parathyroid tumor or idiopathic parathyroid hyperplasia produces metabolic alterations. In the clarification of this problem, the Boston School, led by Albright Churchill, and Cope, played a prominent role.

(*To be continued*)

ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Surgical Treatment of Tumors of the Jaw; Indications for Endobuccal Resection (Tratamento cirúrgico dos tumores da mandíbula indicações da ressecção endobucal). JORGE MARSILLAC. *Rev. brasil. cir.*, 1953, 26: 44.

THE AUTHOR emphasizes the fact that many articles have been published on tumors of the jaw and that the treatment of such tumors should be known both by doctors and dentists.

This article is based on the records of the National Cancer Service, which, up to the time this article was published, recorded 79 cases of jaw lesions under the following classifications:

a. Primary tumors: (1) bone tumors and (2) dental germ tumors.

b. Secondary tumors: (1) metastatic tumors and (2) propagated tumors from nearby structures.

Other classifications are also given, such as the one from the Bone Registry of the American College of Surgeons, the one given in Francisco Fialho's thesis, and that in Thoma's classification.

Due consideration is given to the fact that in addition to the neoplastic lesions of the jaw there are some of infectious, metabolic, and traumatic nature which often make diagnosis difficult.

The majority of jaw tumors grow silently with few but very evident symptoms. Progressive deformation of the mouth by tumor growth, pain, lower lip anesthesia, pathologic fracture, and submaxillary and cervical metastases are the principal symptoms.

The history, age, race, presence or absence of metastases, and many other diagnostic factors are usually not adequate. Therefore, roentgenologic examination and biopsy should always be done.

The need of surgical treatment of a jaw tumor can be determined in various ways, but its histologic nature and duration, the presence of infection, and its diagnosis as to being a primary, metastatic, or propagated tumor should be known as well as the extent of any regional or distant metastases. Special consideration should also be given to the patient's age and general condition.

Regarding treatment, jaw tumors are divided into the benign and the malignant. In case of malignancy one should determine whether the tumor is primary or secondary and if there are regional or distant metastases.

Adamantinomas and a few giant cell tumors are considered as borderline lesions.

Benign tumors, as a rule, show no difficulty with regard to treatment. Fibromas, myxomas, lymphomas, chondromas, osteomas, and dental tumors of epithelial, mesenchymatous, and mixed natures are usually treated by trephining resection, or curettage, electrosurgery also being used occasionally.

The endobuccal approach is always used so that the mucosa can always be sutured.

The endobuccal approach is also used for giant cell tumors, adamantinomas, and even for a great number of malignant tumors of the jaw of the radioresistant type and without cervical node enlargement.

The endobuccal approach in the hands of a qualified surgeon is no more difficult than the extraoral approach. It has the advantage of not leaving an external scar, salivary fistula, or keloid, and does not sacrifice the lower facial nerve terminations, thereby avoiding deformation of the mouth.

For larger tumors of the mouth (even benign ones) and for malignant tumors with lymph node enlargement, the external approach (extrabuccal) gives no alternative of choice.

The author performs all of these endobuccal operations under general anesthesia with intubation and tamponade of the pharynx. Aspiration is always used, and two assistants are required.

In cases of malignant tumors with cervical node enlargement a previous tracheotomy is done and followed by a large cervical node dissection in continuity with a partial jaw resection.

The tracheal cannula is removed 4 or 5 days later and the patient is fed by nasal catheter from the first day.

In cases in which the entire half of the jaw is removed a tracheotomy is also done.

—*Joao B. Vianna, M.D.*

EYE

Blepharoptosis; A General Consideration of Surgical Methods, with the Results in 162 Operations. CARL CORDES JOHNSON. *Am. J. Ophth.*, 1954, 38: 129.

THIS well illustrated, cogent, and comprehensive discussion of blepharoptosis is based on an analysis of 162 operations done at the Massachusetts Eye and Ear Infirmary in the past 10 years. Detailed preoperative study is emphasized. Other lid and extraocular muscle

anomalies should be corrected before the ptosis operation is undertaken.

The results of levator resections are far better in patients with strong superior recti than in those with weak superior recti. Levator resection is indicated in unilateral ptosis if there is the slightest evidence of levator function, or, failing this, if there is strong binocular vision and a good superior rectus. In such cases the author favors his own procedure of levator resection done through the skin surface.

Suspension from the superior rectus by the Berke-Motais method is the operation of choice in either unilateral ptosis with complete levator palsy or in bilateral ptosis with complete levator palsy, provided that the binocular vision is weak and the superior recti are strong. Utilization of the frontalis muscle is necessary in bilateral ptosis with paralytic levators and weak superior recti. The correction of ptosis is most successfully effected by levator resections in eyes uncomplicated by other muscular anomalies, excellent results being obtained in 85 per cent of these cases. —*James E. Lebensohn, M.D.*

Surgery of Carcinomas in the Region of the External Palpebral Commissure (Sobre o tratamento cirúgico dos carcinomas vizinhos da commissura palpebral externa). José Conde and Artur Pina. *Arq. pat.*, 1953, 25: 212.

The anatomy of the region about the external palpebral commissure is reviewed, and the extension of carcinomas in this region into the deep tissues is described. The pathology of basocellular carcinomas in general is reviewed, with particular emphasis on their histologic structure, their malignancy, their resistance to irradiation, and their metastatic routes.

The authors advocate complete excision en bloc of malignant lesions in this region, on the surface as well as in the deep tissues, and prophylactic excision of the cervical glands in any case in which the glands are palpable. Excision of subjacent osseous structures to complete exenteration of the orbit may be done.

The carcinomas of this region are divided into three categories: (1) invasion of the deep tissues involving the bone, muscle, and fascia, without involvement of the orbital contents; (2) involvement of the deep structures and also of the orbital contents; (3) invasion of the orbital contents, without involvement of the bone, muscle, or fascia.

A surgical pattern for each category is outlined, the techniques and their effectiveness demonstrated by reports of cases. —*Ray Karchmer Daily, M.D.*

Metastatic Carcinoma of the Choroid. Olga Sitchevska. *Am. J. Ophth.*, 1954, 37: 873.

The author points out that metastatic carcinoma of the choroid is not common. Only 15 cases were encountered during the last 35 years at the pathologic laboratory of the New York Eye and Ear Infirmary among 4,000 enucleated eyes.

Carcinoma of the female breast is the most common source of carcinoma of the choroid. Next in frequency is carcinoma of the intestines, the prostate, thyroid, ovary, uterus, liver, kidney, and testicle.

Choroidal carcinoma occurs bilaterally in about 25 per cent of the cases.

The prognosis is grave as metastasis to the eye indicates generalized metastases and death occurring in a few months to about 2 years after the ocular lesion.

The author reports a case of carcinoma of the choroid in a woman 64 years of age which had metastasized 5¼ years after the primary growth in the mammary gland. The lesion in the breast had been diagnosed as "infiltrating duct carcinoma grade 2 with metastasis to several axillary lymph nodes." Clinical diagnosis of the ocular lesion was confirmed by microscopic examination of the enucleated eyeball as "metastatic carcinoma of the choroid with beginning invasion into the optic disk."

Although death occurred 15 months after the eye was enucleated, this procedure was justified to avoid pain, secondary glaucoma, or extraocular metastases.

The author advocates routine ophthalmoscopic examination in all cases of carcinoma of any organ of the body. —*Joshua Zuckerman, M.D.*

NOSE AND SINUSES

Olfactory Esthesioneuroepitheliomas of Louis Berger. L. Fruehling and Charles Wild. *Arch. Otolar.*, Chic., 1954, 60: 37.

Due to the origin of the olfactory mucosa, one might expect to find in the nasal fossa tumors bearing a resemblance to those originating in the central nervous system. Berger, in 1924, described a tumor of the nasal fossa with a histologic structure reminiscent of that of the embryonic nerve tumors. Since then others have added to the literature descriptions of these "olfactory esthesioneuroepitheliomas of Louis Berger."

The symptomatology of these tumors is in no way specific; it consists of nasal obstruction, nasal hemorrhage, anosmia, and headache. Examination reveals the tumor, but it is usually not possible to make the diagnosis clinically. The authors emphasize that any slightly unusual or suspicious polypoid formation in the nasal fossa should be subjected to microscopic examination. Failure to make such an examination accounts in part for the rare occurrence of the diagnosis.

Unless the pathologist is aware of the existence of such tumors the histologic diagnosis may be missed. They may be confused with glandular epitheliomas or sarcomas. In addition to pseudoepitheliomatous forms there are pseudosarcomatous forms with spindle-shaped elements, or with lymphocytoid elements, and also polymorphous forms. True neuroepithelial rosettes were observed in 3 of the 4 cases reported by the authors, and typical neurospongial cells were seen in all 4 cases reported. A rigorous histologic technique, with study of the collagen (using Masson's trichrome stain) will aid in arriving at the proper histologic interpretation.

The authors report 4 cases. In each, the tumor was removed by surgery, followed by irradiation of from 4,500 to 6,000 roentgens. The authors believe this to be the preferred method of treatment, and point out that true olfactory esthesioneuroepitheliomas are extremely radiosensitive.

Only 1 of the 4 cases reported could be followed clinically. This patient survived for more than 5 years with good health and no recurrence of the tumor.

—*Fletcher Austin, M.D.*

MOUTH

Plastic Operations for Partial or Total Losses of the Lip. EDUARD SCHMID. *Plastic & Reconstr. Surg.*, 1954, 14: 138.

THE AUTHOR presents a procedure that is useful in reconstructing the upper or lower lips, based on the use of a bipedicled bridge flap from the submental skin.

The anterior incision follows the lower border of the mandible, from the insertion of the masseter muscle on one side, across the chin to the border of the masseter on the other side. The posterior incision parallels the first, with its ends swinging toward the margin of the mandible. The entire flap is formed in one stage and lifted over the chin like a visor. The oral raw surface is covered by inverted skin from the flap, or from previously raised skin flaps from the margins of the lip defect. The defect of the submental donor area is easily closed by advancing the neck skin. The raw surfaces between the lips and the rim of the jaw on the pedicles of the flaps are covered by Thiersch grafts. In the majority of cases sufficient mucosa was obtained from both buccal surfaces to cover the oral raw surface, and in several cases reconstruction of the vermilion border with a tubed mucous membrane flap was performed. If no mucosa is available, the oral surface of the visor flap can be lined with a split thickness graft prior to its transfer. *Earl H. Klabunde, M.D.*

Restoration of Lip Contour Using Fascia, Tendon, and Dermal Grafts; Correction of Flat Lip Deformity. KENNETH PICKRELL, FRANK MASTERS, NICHOLAS GEORGIADE, and CHARLES HORTON. *Plastic & Reconstr. Surg.*, 1954, 14: 126.

IN CORRECTING flat lip deformity, the authors use free fascia, tendon, or dermal grafts to restore contour fullness and "expression." Also, they believe that mobility is improved. While this deformity most commonly follows cleft lip repairs, it may also follow trauma or tumor resection.

While a long strip of fascia lata is probably the graft of choice, a tendon graft, the palmaris longus, the flexor digitorum sublimis from the fourth finger, the peroneus brevis, or dermal grafts were used. The latter are not as satisfactory because of their inability to glide and function as a mobile structure. The fascia strip is cut 1 cm. in width, 18 to 20 cm. in length, and is then folded upon itself to obtain a triple thickness. The fascia lata defect is not closed.

With care not to cause swelling or distortion of the lip, a small incision is made in the skin just superior and lateral to each oral commissure and a tunnel is dissected across the upper lip superficial to the orbicularis muscle. This tunnel is located just above the vermilion border. The triple-folded fascia or double-folded tendon graft is placed through this tunnel. The most important maneuver in the procedure is the placing of the temporary suture in the mucous membrane at the buccal surface of the lip just above the frenulum to retract the lip superiorly under tension, converting it to an exaggerated arc drawing more of the graft into the tunnel. With tension on this suture, the graft ends are anchored to the orbicularis oris and buccinator muscles on each side. The main incisions are closed in a double layer and no dressings are applied.

Grimacing and puckering movements are begun almost immediately and massage of the lip is carried out even before the sutures are removed.

—Earl H. Klabunde, M.D.

NECK

Present Trends in Treatment of Carcinoma of the Larynx. R. G. MACBETH. *Irish J. M. Sc.*, 1954, 6: 141.

THE author lists 88 cases of carcinoma of the larynx, all of which except 13 were treated by him personally. Seventy-four of the patients were subjected to operative treatment, 10 to radiation therapy, and 4 had no treatment at all. This is not a large series when compared with American figures, but cancer of the larynx amounts to less than 2 per cent of all malignant disease, and the publication of such a series may be of some value when it is realized how closely the figures tally with other published reports.

The author states at the beginning of his article that with the present techniques that are available to the surgeon and with the current antibiotics that are at his disposal surgery is preferable to radiation treatment for almost all cases of carcinoma of the larynx, and he sets about to confirm this statement by the figures that he publishes. From the prognostic point of view the best cases for surgery are also the best cases for radiation therapy, and the biggest advantage that the radiologist can adduce is that in successful cases function of the cord is preserved. He also claims that should radiation therapy fail, surgery can then be used. Some surgeons would agree that this is a fair conclusion; others consider that previous irradiation makes subsequent operation difficult and tedious because of the scarring produced, and reconstructive surgery may be impossible because of the diminished blood supply to the skin. Surgery is often capable of salvaging irradiation failures, while the reverse is rarely true. In favor of surgery, it is argued that in early cordal cases the operation of median thyrotomy leaves patients with a voice which is serviceable for most purposes, whereas irradiation may lead to perichondritis or necrosis of the cartilages.

Although the different types of laryngeal carcinoma must be segregated as far as statistics are concerned, the author's over-all 5 year survival rate was found to be 65 per cent as compared to an average of 62.6 per cent in 5 other series. The figures that he has compared with his have been taken from authors in various countries of the world.

The author's choice of anesthetic is endotracheal nitrous oxide-oxygen administered in combination with cervical plexus block and subcutaneous infiltration of the field with a local anesthetic that has adrenalin in it. A U-shaped incision is made. The limbs of this "U" are not extended significantly until it is ascertained whether a radical neck resection is necessary. In general, the operation is radical, and in all cases the body of the hyoid and the strap muscles are taken in order to clear away the lymph-node-bearing tissue in front of the epiglottis. Interrupted fine stainless steel wire is used to close the pharynx. A tracheotomy tube is rarely used as it is better to avoid the use of this tube so that the patient will not rely upon it in the later postoperative period.

Radical neck resection is limited to those cases in which definite involvement of the nodes is found. An exception to this dictum is the case in which a supraglottic, subglottic, or pyriform fossa lesion is encountered, and in such a case a prophylactic radical neck dissection is done routinely at the time of the laryngectomy. The nodes on the opposite side of the neck are not resected routinely in these cases, one waits to see if any enlargement occurs postoperatively before making a decision in this regard.

—*Matthew H. Evoy, M.D.*

CORRECTION.

The following abstract has been prepared to replace a previous one of the same article, which appeared in an earlier issue.

Bilateral Neck Dissection with Excision of Both Internal Jugular Veins and Related Matters. E. S. MYERS. *Med. J. Australia*, 1953, 2: 957.

IN 1923 G. W. Crile recommended block dissection of the neck with excision of both jugular veins so long as there was an interval of several weeks between operations—no matter where the primary lesion was.

In 1931 operation was performed by the author on the right side, and later a second operation was undertaken on the left side. However, the patient died during the operation and a Royal Commission held an inquiry regarding the cause of death.

The Royal Commission found the cause of death was: (1) anesthesia, (2) operation upon the neck, and (3) syncope. He also found that the operation was justifiable to prolong life, that it had been attempted only after careful examination and consultation between experienced medical men, and that the actual operation, so far as it had gone, was performed skilfully and without negligence.

Since the time that Crile's article appeared, Gius and Grier, Ray, Modlin, Royster, and Batson, have written on the subject. The author of this article has set out the points they raised for and against the performance of the second operation, which were based upon the anatomy and physiology of the veins of the region concerned.

More recently Baehrs and Jordan have reported a case and stated, "Since the adequacy of the collateral circulation about the head and neck has been better understood, radical cervical dissection can be carried out without the dangers previously thought to be present when both internal jugular veins were removed."

The article concludes with a description of certain modifications of block dissection of the neck and removal of the internal jugular vein which should make the operation easier of performance.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

The Treatment of Hydrocephalus. DONALD D. MATSON. *Surg. Clin. N. America*, 1954, 34: 1021.

THE author clearly defines hydrocephalus and describes the various types which are encountered clinically. The diagnostic steps recommended include careful head measurement, roentgenography, bilateral subdural puncture to rule out subdural hematoma, combined puncture of the lateral ventricle followed by lumbar puncture with protein determinations of both fluids and followed by the introduction of a dye into the ventricle and determination of its appearance in the spinal canal. Urine studies are also done after the introduction of phenolsulfonphthalein into the ventricles, and ventricular air studies complete the investigation.

Early therapeutic measures are recommended, whenever possible, before irreversible damage of the central nervous system has taken place.

The various types of treatment which have been employed are discussed and the measures particularly used by the author are described in more detail. These include ventriculocisternostomy, third ventriculostomy, shunts from the lateral ventricle into the mastoid antrum, the pleural cavity or peritoneal cavity, or ureter. Each of these procedures is discussed with regard to the technical problem and the results that may be expected. In communicating hydrocephalus the best results have been reported as following a lumbar subarachnoid ureteral shunt. The cases of 65 patients who had been subjected to this operation were reported with a postoperative follow-up for 5.5 years. Forty-five of the patients were living and 36 of these were in good health and exhibited normal or only slightly retarded development.

Lumbar subarachnoid peritoneostomy is also discussed, but the problem of keeping the tube open has been greater than it is in the ureteral shunt.

Other special types of hydrocephalus include atresia of the foramina of Magendie and Luschka, adenoma of the choroid plexus, and Arnold-Chiari malformation.

The diagnosis and methods of treatment for these conditions are also discussed.

Early recognition of the condition and the institution of appropriate treatment before serious brain damage has taken place are important. In the later cases with obvious serious retardation only custodial care is advised. —*Howard A. Brown, M.D.*

Cerebral Angiography in the Diagnosis of Intracranial Lesions. OSCAR SUGAR. *Surg. Clin. N. America*, 1954, 34: 1051.

THE value of angiography in the diagnosis of intracranial lesions is outlined by the author and it is believed that the performance of angiography following subarachnoid hemorrhage does not increase the immediate hazard. However, in view of the hazards associated with the early treatment of intracranial aneurysms after bleeding, it is thought that angiography should be delayed until hemorrhage has subsided. In the study of aneurysms it is believed that negative studies should be repeated in a week or two in the hope that an occluding clot may have retracted or vasospasm has diminished, to allow the visualization of an aneurysm which previously was undisclosed.

Arteriovenous malformations are often characterized by convulsive seizures with perhaps a lesser tendency to bleed than aneurysms, and they can often be identified by cerebral angiography. Such studies often allow an extensive removal of the malformation with subsequent recovery.

In arteriosclerotic or occlusive vascular disorders, angiography again is of considerable value in localizing the condition as well as in allowing one to come to a definite diagnosis as to the type of process present.

It was thought that the use of cerebral angiography in the diagnosis of space-occupying lesions might be more debatable. However, certain information may be obtained with reference to the filling of blood vessels within the tumor or the lack of filling in cystic and purulent collections, which might not be visible in pneumoencephalograms. A diagnosis of space-occupying lesions above the tentorium was possible in 75 per cent of the author's patients without knowledge of the history. The type of lesion to be anticipated was forecast accurately in about 50 per cent of the patients.

Some discussion is given to the problem of abscess localization and it is thought that angiography is of distinct value.

The dangers of angiography are also considered and it is thought that with improved technique and the need for less injection the risks are smaller than previously had been the case.

It was thought that angiography could not completely replace other diagnostic methods but must be used as an adjunct in many instances.

—*Howard A. Brown, M.D.*

The Pathology of Spontaneous Intracranial Hemorrhage. DOROTHY S. RUSSELL, M. A. FALCONER, DIANA J. K. BECK, and W. H. MCMENEMEY. *Proc. R. Soc. M.*, Lond., 1954, 47: 689.

IN ONE series of 461 patients, the authors found the following pathologic conditions responsible for spontaneous intracranial bleeding: hypertension, 232 cases; congenital medial defects in cerebral arteries (92 cases with aneurysm), 96; blood diseases (acute leukemia, thrombopenia, aplastic anemia, etc.), 36; mycotic aneurysm, 28; vascular hamartoma (telangiectases, cavernous hemangioma, arteriovenous malformation), 21; arteritis (no aneurysm, no polyarteritis nodosa, but rather, instances of purulent inflammation), 13; neoplasms, 9; arterial degeneration (no cardiovascular hypertrophy), 7; various other conditions, 3; cause never found, 16. By far the commonest site of hemorrhage in the patients with hypertension was found to be the basal ganglia.

It is pointed out that the spontaneous rupture of aneurysms is usually a matter of seepage through a

necrotic site in the wall of the lesion, and that even a small amount of blood, especially its bilirubin content, can cause severe meningeal signs, such as the original clinical symptoms of severe pain in the head. Actual rupture, with torrential bleeding, is never compatible with life. Aneurysms are lesions of the middle age groups.

Arteriovenous malformations manifest themselves more often by epilepsy than by hemorrhage, but when they do bleed the clinical picture is often indistinguishable from that of a leaking aneurysm. Any differences are qualitative rather than absolute. The association with epilepsy, the occurrence of bleeding in childhood, or a history of attacks of bleeding extending over many years is more suggestive of malformation than of aneurysm. These lesions are basically arteriovenous fistulas. Many vascular defects of the various possible types may not be demonstrated by the best of arteriograms. —*John Martin, M.D.*

The Treatment of Ruptured Intracranial Aneurysms. WALLACE B. HAMBY. *Surg. Clin. N. America*, 1954, 34: 1063.

THIS article is confined to the ruptured "berry" type of aneurysm about the circle of Willis.

It is thought that cerebral angiography should be performed as soon as the patient's clinical state permits. The percutaneous method with intravenous sodium pentothal anesthesia is recommended as the safest plan.

Medical management is discussed; this consists chiefly of bed rest, supportive medication, nutrition of adequate type, and symptomatic medication. Previous reports on the management of this type of aneurysm indicated that patients who survived the initial hemorrhage had an 80 per cent chance of carrying on for some years without disabling symptoms and without recurrence of hemorrhage.

In the author's series previously studied, 48 per cent of the patients died in the hospital and 22 per cent of the survivors had died by the time the survey had been completed.

The various surgical measures of treatment are considered, including carotid ligation, direct attack upon the aneurysm, and trapping of the aneurysm. Some detailed consideration is given to each of these methods.

The surgical approach as used by the author for aneurysms in various locations is described.

It was thought that it was quite difficult to determine from various reported series whether in the acute stage following bleeding it is safer to tie the artery in the neck or to occlude the aneurysm intracranially. If the two procedures presented about the same degree of risk the author believed that the intracranial attack was desirable, as it gave a better chance of permanent cure.

Some statistics are offered regarding the direct approach to the aneurysm. This was done in 38 patients, of whom 22 survived, a mortality rate of 42 per cent. Fifteen patients were treated by cervical ligation of a carotid artery in addition to an intracranial attack with a mortality of 27 per cent. Twenty-three patients were treated by intracranial operation without cervical ligation with an operative mortality of 52 per cent.

It is thought that operation should be deferred for 2 or 3 weeks following the last hemorrhage as the mortality can be reduced by this delay.

It is suggested that further work be done in an attempt to find a means of temporary occlusion of the carotid artery in the neck without intimal damage to allow for temporary protection against intracranial bleeding with the possibility of subsequent re-establishment of the arterial channel.

—*Howard A. Brown, N.D.*

Cerebellar Astrocytomas (Astrocitomas del cerebelo). S. OBRADOR ALCALDE. *Cir. gin. urol.*, 1954, 7: 229.

THE author discusses astrocytomas of the cerebellum by analyzing the American literature almost exclusively, in conjunction with his own series of 23 cases. In general, his conclusions parallel closely those of previously reported series.

Of the 23 patients, 2 children, 2 and 4 years old respectively, presented a picture interpreted as hydrocephalus, and they were palliatively ventriculostomized, the diagnosis of cerebellar astrocytoma being made post mortem. Of the remaining 21 patients, all were subjected to suboccipital craniectomies through the classical curved transverse incision, with complete removal of the tumor and with an operative mortality of 14 per cent.

In the author's material, the mean age was from 10 to 15 years. Three patients were younger than 10 years and 2 were more than 30. The author was impressed with the short duration of the symptoms (less than 1 year in 14 patients), a fact which made the preoperative differential diagnosis from malignant neoplasm difficult. The symptoms and signs recorded agree with the classical experience, but the author remarks on the paucity of limb ataxias despite the frequency of hemispheric invasion, although 14 patients had locomotor ataxia. Only 10 patients were subjected to ventriculography. An electroencephalogram was done in 6, marked abnormalities being encountered in 3. All 21 patients showed papilledema preoperatively, and in some it had already been replaced by secondary optic atrophy.

The author advocates radical excision. He reports varying degrees of cystic change in 20 of his 23 patients. Two of his patients had been operated upon elsewhere 10 and 2 years previously, respectively, by mere evacuation of the cystic contents.

Brain stem syndromes may occur postoperatively, particularly when the tumor is intimately attached to the vicinity of the floor of the fourth ventricle; the syndromes may be external ocular muscle disturbances, bulbar paralysis, facial diplegia, as well as the exacerbation of a preoperative cerebellar deficit. The observation was made that the bulk of these postoperative neurologic dysfunctions tend to disappear or attenuate within a reasonable time. Aseptic meningitis occurred often and required frequent lumbar punctures.

Histologically, the author considers cerebellar astrocytomas as more uniformly benign than their supratentorial counterparts. Only 3 specimens showed any sort of atypical feature, and 1 specimen exhibited mitotic figures.

Aside from the mortality rate mentioned, no patients have shown evidence of recurrence, 11 have negligible

symptoms or are asymptomatic, and of the 7 with symptoms, 6 are blind and 1 is frankly ataxic. The period of observation ranges from less than a year to 4 years.

The author's total series of 800 expanding intracranial lesions were broken down as follows:

Tumors	500
Vascular lesions (hemangiomas, aneurysms)	57
Tuberculomas	38
Cysticercosis	21
Abscesses	17
Hydatid cysts	16
Hydrocephalus and "pseudotumors"	151

Among the cerebellar tumors, the astrocytoma was fourth in frequency, the medulloblastoma, acoustic neurinoma, and tuberculoma preceding it in that order. —*Juan E. Fonseca, M.D.*

PERIPHERAL NERVES

Peripheral Nerve Injury. BARNES WOODHALL. *Surg. Clin. N. America*, 1954, 34: 1147.

THE author discusses certain fundamental prerequisites for successful peripheral nerve repair and in so doing describes the structure of the peripheral nerves, Wallerian degeneration, and the acute pathology of peripheral injury. The importance of the mesenchymal reaction about the nerve in relationship to axonal regeneration is stressed as is the difference between surgical and traumatic division of the peripheral nerves, especially insofar as the diffuse nature of nerve damage due to stretching is concerned in traumatic lesions. The various types of injuries characterized by incomplete nerve section as well as their pathologic changes are described.

Repair of nerve injuries may be done during the acute period or later, after the healing of the initial wound, which may be termed a delayed nerve suture. So called "late suture" is that done after about 3 months when degenerative changes in the distal parts tend to compromise the final result. A few of the advantages of deferred nerve suture are those gained by the patient's ability to stand a possibly long anesthesia, the decreased risk of infection, the better condition of the surrounding tissue, and the better delineation of the pathologic area. There is also the advantage of a period of grace given the occasional operator to inform himself of the anatomy of what might otherwise be a foreign field. The disadvantages of such delay are the necessity of two anesthetics and the loss of some several weeks insofar as axonal regeneration is concerned.

Methods of motor and sensory testing are described as are the more pertinent electrical studies and their interpretation. The author again stresses the general principles of peripheral nerve repair, i.e., the use of properly planned generous incisions to give adequate mobilization of the nerve so as to avoid suturing under tension, and the use of fine, nonabsorbable suture material. The use of electrical stimulation at surgery is suggested as a valuable aid, and because of this, the author thinks it wise to use a local anesthetic when possible. The difficulties in deciding whether or not to resect a partial lesion which appears to be a neuroma in continuity are discussed as well as the criteria for resection. Resection well beyond the limits of scarring is necessary if good recovery is to be achieved. Proper splinting during the postoperative period is required. Adequate use of physiotherapy will prevent much loss of joint motion and contractures. Finally, should nerve repair be impossible, inadequate, or otherwise fail, tendon transfers may be done to salvage function.

—*Nicholas Wetzel, M.D.*

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SURGERY OF THE THORAX

CHEST WALL AND BREAST

The Fascia of the Breast and Axilla. E. S. MEYERS. *Med. J. Australia*, 1954, 1: 966.

NEARLY all skeletal muscle is enveloped by a layer of fascia. Sometimes the fascia is a prominent structure and at other times it is a very thin enveloping membrane. Where muscles are in contiguity or where they overlie one another, the fascial layer separating two muscles is common to these two muscles.

The fascia covering the anterior aspect of the pectoralis major is rather thin, while the fascia on the deep surface is strong. The coracoclavicular fascia is a strong fascia which occupies the interval between the pectoralis minor and the subclavius and protects the axillary vessels and nerves. Medially it blends with the fascia covering the first and second intercostal spaces, and laterally it is attached to the coracoid process. This is sometimes called the costocoracoid ligament. Below this, it consists of a thin layer and gives a covering to the anterior and posterior surface of the pectoralis minor. It then continues downward to join the axillary fascia and is sometimes known as the suspensory ligament of the axilla.

The fascia over the serratus anterior is firmly attached, and in stripping it off the muscle care must be taken or the nerve to the serratus anterior may be damaged. The fascia over the subscapularis is a thin membrane and may be stripped with ease, but again care must be exercised or the nerve to the latissimus dorsi may be injured.

The fascia over the short head of the biceps, the coracobrachialis, the lattisimus dorsi, and the teres major can also be stripped with ease.

The axillary fascia extends between the lower border of the pectoralis major anteriorly and the latissimus dorsi posteriorly. The axillary sheath forms the connecting channel between the neck and the axilla as it envelops the great arteries and nerves as they extend from the neck into the axilla.

—John H. Davis, M.D.

The Technique of Extrafascial Radical Mastectomy. HUGH R. G. POATE. *Med. J. Australia*, 1954, 1: 967.

A DETAILED technique for performing radical mastectomy for carcinoma of the breast, based on an exact knowledge of the axillary fascia, is presented. The method is an improvement over the original Halsted technique and is based on the description of the axillary fascia as given by E. S. Meyers. Each muscle has its own fascial envelope which surrounds the muscle and this envelope gives off sheaths to cover blood vessels and nerves or to overlie potential spaces, such as the floor of the axilla. The axillary fat and lymph glands lie within a fascial cone which extends up along the axillary sheath to enter the lower part of the posterior triangle of the neck. This course provides a pathway for the axillary lymph vessels to join the thoracic duct or the right lymphatic trunk. The maintenance of the integrity of this fascial cone which surrounds the axillary fat, lymph glands, and lymphatic vessels is the essential feature of the operation.

A detailed, illustrated description of the operation is provided, with emphasis on the incision and removal of the enveloping axillary fascial cone so that adequate removal of the lymphatic drainage can be obtained. The technique minimizes the risk of "milking" carcinoma cells along the lymphatic vessels.

—John H. Davis, M.D.

TRACHEA, LUNG, AND PLEURA

The Surgical Treatment of Patent Ductus Arteriosus; a Review of 50 Cases. IRENE S. CADE. *Brit. J. Surg.*, 1954, 42: 31.

IN ENGLAND, following the trend in the United States, the indications for surgical correction of patent ductus arteriosus have been broadened. The author favors elective closure of the ductus to prevent the complications of it, and to lessen the increased surgical risks of complicated cases. The exception is the older patient, in whom the risks are greater. Surgery should not be elected in the absence of symptoms. When feasible, operation should be performed on the patient who is between 5 and 10 years old.

It is believed that ligation of the ductus, as it was performed in 48 of the 50 cases here presented, is safer than, and equally effective as, division and suture. An analysis of the clinical features of the 50 cases indicated that 21 had symptoms varying from those caused by cardiac overwork to those of bacterial endocarditis. There were no deaths due to the operations.

Of particular interest were follow-up studies among 29 patients who had denied having symptoms before surgery. Seventeen patients noted an increased tolerance for activity for 7 months to 7½ years after operation; and only 1 patient has any symptom (slight breathlessness on heavy exertion) that may be referable to her operation in some unknown way. Of the patients with preoperative symptoms, only 1 has not become markedly improved.

—Leonard D. Rosenman, M.D.

Reduction of Pulmonary Reserve; Technique for Reducing Pulmonary Capacity to 15 Per Cent, with Measurement of Right Heart Pressures and Arterial Blood Oxygen Saturation in Dogs at Rest and During Exercise. A. FLORES, W. E. ADAMS, and J. F. PERKINS, JR. *Arch. Surg.*, 1954, 68: 627.

THE authors describe a method (in vivo) of occluding a bronchus, a pulmonary artery, or both, in order to produce a shuntlike effect, a diffusion difficulty, or pulmonary hypertension. The principle involves use of a pneumatic "occlusion unit." The device consists of a polyethylene bag connected to a polyethylene tube. The bag is sewn around the bronchus and pulmonary artery, and, when inflated with a syringe, will completely occlude the vessel or bronchus.

A method was described for reducing the lung capacity in dogs to 15 per cent of normal. With the

use of a Cuvette oximeter, a Rahn alveolar sampler, and a catheter in the right ventricle, the altered physiological effects were demonstrated.

—*Harold L. Method, M.D.*

The Surgical Treatment of Bronchial Asthma by Modified Operative Procedure. J. DANIEL SZOKODI. *Ind. J. Surg.*, 1954, 16: 152.

IT IS ASSUMED that the vagus and the thoracic sympathetic nerves provide sensory and motor fibers to the lungs, and both play a role in the bronchoconstriction of asthma. Bilateral extrapleural thoracic sympathectomy extending from the second to the fifth ganglia, and transection of the pulmonary vagal branches were performed in a series of 14 patients with intractable bronchial asthma. The operation is first performed on the right side through the fourth intercostal space. The homolateral and contralateral branches of the vagus from the recurrent nerve down to the pulmonary ligament are transected. Sympathectomy is performed through the same incision with the patient brought into the semilateral position. Operation on the left side is performed 1 to 3 months later with the thoracotomy incision moved down to the fifth intercostal space.

There was no operative mortality, but spontaneous pneumothorax occurred in 2 patients. For the short follow-up period of 1 year these patients were free of severe asthmatic attacks.

B. G. P. Shafiroff, M.D.

Tubercle Bacilli in Pulmonary Lesions After Treatment by Chemotherapy and Excision; Study of 97 cases (Le bacille de Koch dans les lésions tuberculeuses traitées par exérèse après chimiothérapie; une étude de 97 cas). G. CANETTI, R. ISRAEL, P. HERTZOG, P. DAUMET, and L. TOTY. *Poumon*, 1954, 10: 465.

A STUDY was made of resected specimens of 97 patients with pulmonary tuberculosis. Ten specimens were obtained by pneumonectomy, 54 by lobectomy, and 33 by segmental resection. The lesions were studied by means of culture.

Nine patients had no preoperative chemotherapy or had an undetermined amount. Eighty-eight patients received streptomycin, isoizaide, para-aminocalicylic acid, or more than one of these agents in combination.

At least four cultures were made for each patient, 381 in all. Of these, 48.6 per cent were positive, 43 per cent were negative, and 8.4 per cent were unsatisfactory because of contamination. In 27 per cent of the patients no positive culture was obtained from any lesion, and in 70 per cent at least one lesion was positive. (In 3 per cent of the patients the cultures were contaminated.)

The tuberculous lesions were of three types: nodules, tuberculomas, and cavities. There was a total of 171 nodules. Cultures were positive in 88 per cent of the nonencapsulated caseous nodules, in 70 per cent of the nodules containing areas of liquefaction, and in 40 per cent of the encapsulated nodules. The percentage of positive cultures was about the same for nodules of recent duration and for nodules that had been present a long time. The duration of chemotherapy had no relationship to the positive character of the cultures of the nodules.

Twenty-four tuberculomas removed from 21 patients were studied. Fifteen tumors (62%) gave positive cultures and 9 cases (38%) gave negative cultures. The incidence of positive cultures was higher for large tuberculomas than for small ones. Tuberculomas were similar to nodules in that when caseation or liquefaction was present a higher incidence of positive cultures was obtained. Also, the effect of chemotherapy on the presence of bacteria in these lesions was inconsequential, and the duration of chemotherapy had no relationship to the positive character of the cultures.

Seventy-seven cavities in 69 patients were studied. Ninety-one per cent of the open cavities (35) communicating with the bronchi gave positive cultures; 63 per cent of the cavities partially filled with fluid (19) had positive cultures; whereas only 13 per cent of the cavities completely filled with fluid (8) had positive cultures. The negative character of the cultures in this type of lesion was related to the duration of the chemotherapy. Thus, in patients treated less than 4 months, 18 per cent of the cavities gave negative cultures, whereas the cavities in patients given chemotherapy for 8 months or more, 54 per cent gave negative cultures.

The principal conclusion reached after this work was that chemotherapy does not affect the incidence of organisms in nodules or tuberculomas, but it has a marked effect on the presence of bacteria in cavities.

—*Frederick W. Preston, M.D.*

Resection of Bronchus and Bronchotracheal Anastomosis in Tuberculous Bronchial Stenosis; Report of a Case (Zur Bronchialresektion und bronchotrachealen Anastomose bei tuberkuloeser Bronchialstenose; Bericht eines Falles). CLARENCE CRAFOORD, V. O. BJORK, and H. HILTY. *Thoraxchirurgie*, 1954, 2: 1.

IT IS ESSENTIAL in the surgery of lung tuberculosis to preserve as much properly functioning lung tissue as possible. In view of the great variety of morphological conditions in tuberculosis of the lung, surgical management is directed to tuberculosis of lung parenchyma or tuberculosis of the tracheobronchial tree.

However, differentiation is made between bronchial tuberculosis, which is mainly influenced by the lung process, and bronchial tuberculosis which occurs independently from the lung disease.

Indications in surgery of the tracheobronchial tree seem more simple and opinions do not vary as much as in parenchymatous lung disease.

Conservative treatment over many years (pneumothorax, thoracoplasty, etc.) does not always result in complete cure of narrowing bronchial disease, even though complications such as atelectasis, mediastinal deviation, or bronchopneumonia may not be observed. According to the experiences of Brunner (quoted in the paper), thoracoplasty in cases of tuberculous bronchial stenosis should be limited to stenosis of the upper lobe bronchus and bronchial tuberculosis due to cavernous lung disease only. For any other type of disease he recommends lobectomy (if one lobe is affected) or pneumonectomy (for total atelectasis).

The authors discuss and report a case of cavernous tuberculosis of the upper lobe with marked stenosis of

both the right main bronchus and the right upper lobe bronchus. In this particular case surgery was aimed at the possibility of preserving as much properly functioning lung tissue as possible. Resection of a minimum amount of lung tissue was possible by performing a bronchotracheal anastomosis. It must be borne in mind, however, that scar formation can follow in the area of the anastomosis. A disadvantage of this kind does not necessarily have to occur and should not be a contraindication to reconstructive surgery within the tracheobronchial tree.

The complete history of the patient in question, and the management and description of the operative procedure are given in detail. It is important to note that resection of the right stem bronchus was carried out from the carina down to approximately 1 cm. above the point at which the middle lobe bronchus comes off. A temporary prosthesis by means of a connecting tube maintained ventilation of both the right middle lobe and right lower lobe during the operation. The trachea and the distal bronchial opening were reunited with single mattress sutures. After the anastomosis was finished, tested, and found airtight, a pleural flap was used to cover the area of the anastomosis on the outside.

In the postoperative period the patient showed a rapid recovery. Control examination after a period of 1 year showed an overall excellent functional result. Bronchoscopy revealed an opening of 9 mm. diameter towards the right lung at the site of the anastomosis.

—*Edith Simandl, M.D.*

The Local Treatment of Acute Pulmonary Abscess (Die lokale Behandlung des akuten Lungenabszesses). E. Bauer. *Wien. med. Wschr.*, 1954, 104: 557.

The author presents the history of 2 cases of lung abscess. The etiology in both instances was the aspiration of substances during a long period of unconsciousness after an attempt at suicide.

Endobronchial treatment at an early stage i.e., in the presence of a thinwalled membrane around the abscess which still enables the cavity to collapse, consisted of repeated emptying of the cavity and the instillation of penicillin. Both patients were discharged completely cured.

A larger series of patients is mentioned, but no figures are given. —*Edith Simandl, M.D.*

Lipoid Granuloma of the Lung. Rollin A. Daniel, Jr., and Thirwell M. Nolen, Jr. *Am. Surgeon*, 1954, 20: 849.

The authors present 7 cases of lipoid granuloma of the lung. In 5 of the patients the lesion appeared so much like that of a carcinoma that pneumonectomy had to be undertaken. Lesions of this type are being encountered with greater frequency, and, with the coincident increasing frequency of neoplasms of the lung, a real problem in differential diagnosis may be posed. Infantile types of the disease are usually of relatively short duration and more violent than the adult type, which forms the basis of this report. In the adult type the inflammatory changes which accompany the prolonged reaction to the presence of the foreign material constitute a true granuloma with permanent damage to the lung.

The pathologic changes in the lung develop insidiously. On reaching the alveoli the oil is engulfed, in small droplets, by the macrophages. Later a reticulum of collagenous fibers develops around the macrophages so that the oil gradually becomes fixed in fibrous tissue with obliteration of many air spaces. Some of the oil reaches nodes in the region of the hilum and produces enlargement and subsequent fibrosis. This is one of the features which makes it difficult to distinguish the lesion from carcinoma. Repeated ingestion of mineral oil is probably a causative factor; its use as a laxative, particularly at bedtime, must be condemned, as the likelihood of aspiration is great.

—*Benjamin F. Lounsbury, M.D.*

Changes in Shape and Site of Intrathoracic and Extrathoracic Organs After Pneumonectomy, and Their Clinical Significance (Form- und Lageveraenderungen intra- und extrathorakal gelegener Organe nach Pneumonektomie und deren klinische Bedeutung). M. Wenzl and E. Strahberger. *Langenbecks Arch. u. Deut. Zschr. Chir.*, 1954, 278: 248.

The authors, of the Second Surgical Hospital of the University of Vienna, Austria, examined a series of 80 pneumonectomized patients to determine the changes in the shape and site of intra- and extrathoracic organs, and the functional disturbances caused by deviation of the mediastinum. The interval between the pneumonectomy and the examinations varied between 1 year and 7 years.

In 64 cases the pneumonectomy was performed because of bronchial carcinoma, and in 16 cases because of benign conditions. In 62 cases the residual cavity after removal of the lung was left untreated, in 13 cases the phrenic nerve was crushed during the operation, and in 5 cases a plug of "polystan Rx" was inserted in the pleural cavity.

The shift of the mediastinum was determined by measuring the angle of deviation of the trachea from the midline in the anteroposterior roentgenogram. The angle was between 0 and 30 degrees in the majority of cases; only in a few cases was it between 30 and 60 degrees. There was no significant difference in the amount of deviation after right and left pneumonectomy. The esophagus was displaced frequently towards the operated side and often dilated. After left pneumonectomy the diaphragm was displaced cranially by 6 cm. (average), whereas no significant change of the diaphragmatic level was observed after right pneumonectomy.

In 39 of the 80 cases severe changes of shape and site of the stomach were observed. If, after left pneumonectomy, the diaphragm is displaced cranially, the stomach is pulled by perigastric adhesions into the diaphragmatic dome. At the same time the duodenal bulb is displaced to the left; this led in some cases to a rotation of the stomach by 180 degrees so that the great curvature faced cranially.

No definite relation could be established between the degree of deviation of the mediastinum and functional disturbances. The clinical condition and cardiopulmonary function was evaluated by the stair-climbing test and by the "apneic pause" test in combination with oxygen saturation determination during the apneic pause. Among the cases with moderate

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 1 (Wenzl, Strahberger). Dilatation of the esophagus after right pneumonectomy.

FIG. 2. Elevation of the diaphragm after left pneumonectomy. The duodenal bulb is displaced to the left and approximated to the cardia. The stomach is rotated by 180 degrees and the great curvature attached to the dome of the diaphragm.

FIG. 3. The white lines indicate the angle of deviation of the trachea; it is 45 degrees. In spite of this considerable distortion the patient was fully able to work.

mediastinal deviation (among 30 degrees) there were about as many with good as with poor function; and even the majority of patients with extreme deviation showed a satisfactory function. On the other hand, patients were observed who had quite poor function and became dyspneic after a short walk although no deviation of the mediastinum was present. Also, in those cases in which crushing of the phrenic nerve or insertion of polystan in the pleural cavity was done, there was no significant parallelism between the position of the mediastinum and the clinical picture.

The authors draw the conclusion that corrective surgery for mediastinal deviation should be performed only in those rare cases in which a deterioration of the clinical condition is observed within 6 months after pneumonectomy together with an increase of the mediastinal deviation.

—*Werner M. Solmitz, M.D.*

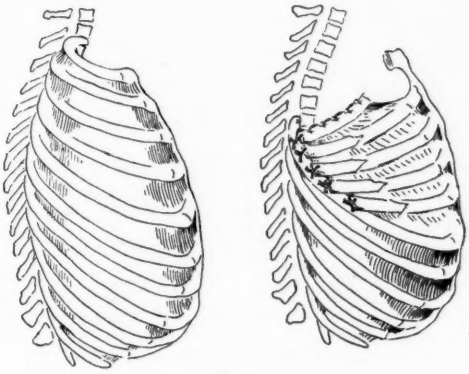


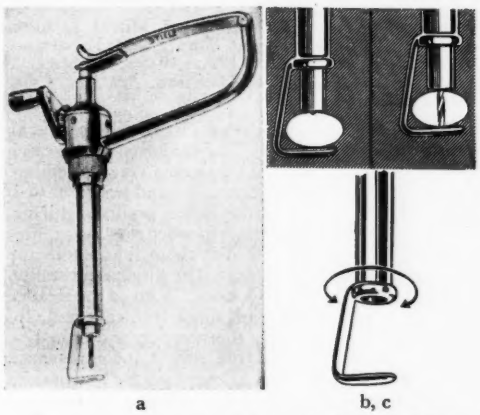
FIG. 1.

FIG. 1 (Björk). The ribs that were parallel have been brought to converge on the posterior part of the sixth rib.

Thoracoplasty; A New Osteoplastic Technique. VIKING OLOV BJÖRK. *J. Thorac. Surg.*, 1954, 28: 194.

A NEW TECHNIQUE for thoracoplasty performed in 118 patients is presented. There was only 1 postoperative death. The new thoracoplasty procedure (Fig. 1) includes: (1) resection of the posterior parts of the ribs; (2) apicolysis to the hilum; and (3) fixation of the ribs to the posterior part of the sixth rib with stainless steel wires placed through drill holes made with an improved, specially designed drill bore (Fig. 2). When the sutures are tied to the sixth rib, the costal cartilages are bent and a stable roof is obtained.

With this new thoracoplasty, paradoxical movements are excluded and cough is much more effec-



a b, c

FIG. 2. a, To make the holes in the ribs a specially designed drill bore is used (Stille, Sweden). b (above), This bore does not slip off the rib and the lung is protected. c, It can be turned in any direction without changing the grip of the hand.

tive. When used as a procedure per se, as much as a seven rib thoracoplasty can be tolerated in one stage. A combination of resection with this type of thoracoplasty is also a well tolerated procedure.

—*John E. Karabin, M.D.*

HEART AND PERICARDIUM

The Surgical Problem of Mitral Insufficiency (Le problème chirurgical de l'insuffisance mitrale). P. CHALNOT, R. BENICHOUX, and C. CHARDOT. *Lyon chir.*, 1954, 49: 552.

THE AUTHORS report on their experience with 30 dogs in which they created mitral insufficiency by a transventricular surgical approach to the mitral valve. In 22 of these dogs the defect was treated by the insertion of a prosthetic device consisting of a plexiglass ball valve to which was attached a lock-nut on a stem. The ball was fixed under the posterolateral mitral valve by means of a transventricular approach. Eleven of the animals died, the most frequent cause of death being thrombosis originating on the surface of the prosthesis, which was associated with displacement of the prosthesis. In 3 of the dogs that died the ball valve was found in the auricle and in 3 others it was floating in the ventricle at autopsy.

Eleven dogs survived the operation. Two are living less than 2 months since the operation; 4 have lived longer than 6 months. The longest survivor has lived 11 months since the operation. The surviving animals appear healthy and are normally active.

Five animals were sacrificed between the second and third postoperative month. Autopsy of these animals showed that the ball valve mechanism was fixed by fibrous connective tissue to the endocardium with a minimum of tissue reaction.

The details of the construction of the valve are given by the authors, and the device is compared to similar prostheses designed by Harken and others.

—*Frederick W. Preston, M.C.*

Results of Surgical Treatment of Mitral Stenosis (Resultados del tratamiento quirurgico de la estenosis mitral). G. DUSSAILLANT, J. ALLAMAND, W. SUNKEL, A. DEL VALLE, and R. CARRASCO. *Rev. med. Chile*, 1954, 82: 92.

THE AUTHORS report their results in 43 cases of mitral stenosis treated surgically. The majority of the cases were very far advanced. In 2 cases a cerebral embolism occurred during the operation and was fatal in 1 of them. In 9 cases auricular flutter occurred during the postoperative period but responded readily to quinidine in 7 patients, but in 2 others who did not tolerate the drug it became permanent. The surgical mortality amounted to 7 per cent (3 cases). Two of the deaths were from heart failure with shock (central type). In 1 case only an exploratory thoracotomy was done because of an associated large mitral incompetence. Seven patients have been followed up for less than 3 months. The late results were studied in the remaining 32 cases. Two patients died a short time after the operation, one of them suddenly during a rheumatic crisis and the other from a recurrent cerebral embolism. The remaining 30 patients have been followed up from 3 to 18 months after the operation.

Improvement in the patient's condition was functional rather than in the condition of the anatomical lesion. It occurred especially with regard to dyspnea (its various types), hemoptysis, and "forward failure." Poor results were obtained in right heart failure, especially when associated with auricular flutter. The latter was not influenced by operation. The auscultatory and palpatory findings in mitral stenosis were extensive but decreased in the majority of cases. Electrocardiographic improvements were also noted, and to a lesser extent there was improvement in the roentgenological findings.

A study of the results from the functional and anatomoclinical point of view showed great improvement in 56.2 per cent of the cases and medium improvement in 15.6 per cent—a general improvement of 71 per cent. There was only slight improvement in 9.4 per cent and no improvement in 3.1 per cent; in 9.4 per cent of the cases the patient's condition became worse. Shortly after the operation there was a death rate of 6.2 per cent. The benefits, in great part, were spectacular even in very advanced cases (terminal). The best results were obtained in subjects with sinusoidal rhythm but without great heart enlargement, in those without any other mitral lesion in association with the stenosis, and in those with no signs of rheumatic activity. The factors that caused 28 per cent of the poor results were heart enlargement, organic modifications of the lungs, auricular flutter, rheumatic states, insufficient operative dilatation of the mitral stenosis, associated aortic incompetence, aggravation of the mitral incompetence, and cerebral embolism.

Two of 3 deaths occurred in very severe cases and the operation shortened life only slightly.

Operation should be performed only in cases of major mitral stenosis without, or with only slight, mitral incompetence. Patients with advanced cases and a large heart, auricular flutter, or minor or medium aortic incompetence should not be refused the benefit of operation. In spite of the risk, great benefit may be obtained.

The following factors will lead to better results:

a. Technical progress: instrumental dilatation when digital dilatation is not enough, and prophylaxis of cerebral embolism.

b. Strict teamwork between the physician and surgeon, and a cardiologist as part of the operating team. The latter's judgment in the selection and preparation of patients for operation should be decisive. Electrocardiograms of the patients should be taken during the operation and also on the following days. Bronchial permeability should be maintained and serial roentgenograms of the thorax taken postoperatively for the diagnosis and proper selection of treatment of pulmonary atelectasia. Parenteral fluid should be given cautiously as patients with mitral stenosis can easily develop pulmonary edema and congestive heart failure. When postoperative shock develops without apparent cause the possibility of a central pathogenesis (cardiac) should be considered. If this is the case, parenteral liquid should be avoided.

c. Proper consideration of rheumatic states. It is very important always to remember that surgery corrects mechanical lesions and that the rheumatic condition cannot be favorably influenced by it. Only in

cases of great emergency should patients be operated on in less than 4 months following rheumatic activity, and means to avoid reactivation of the rheumatic state during the postoperative period should be employed.

Rheumatic activity presents a great risk and leads to poor results. In 1 fatal case, fusion of the mitral operative incision was demonstrated. Current diagnosis of latent rheumatic activity is still far from perfect and new laboratory methods should be employed. Patients operated on for mitral stenosis show an abnormal red cell sedimentation rate curve, the cause of which is not quite clear up to the present time. Nine (22%) of the cases presented a true rheumatic state postoperatively.

d. Routine preoperative and postoperative anticoagulant treatment as a prophylaxis of cerebral embolism.

e. Adequate treatment of auricular flutter. When this condition comes on during operation or during the postoperative period there is no tendency toward spontaneous regression, and it should be treated with quinidine or procainamide. When these drugs are ineffectual, digitalis should be administered (tachyrhythmia).

The authors agree with the general opinion that surgery has completely changed the life expectancy of patients with mitral stenosis and that the results obtained are good as a rule. This conclusion is still justified in spite of the possibility of a gradual narrowing of the orifice after the operation. One may say that with surgery many lives can be saved, suffering is lessened, and many invalids are benefited.

Finally, in the event that stenosis recurs a new operation will be possible. —*Joao B. Vianna, M.D.*

Intracardiac Thromboses (Les thromboses cardiaques chirurgicales). ROGER LETAC, ROBERT CAMAIN, PIERRE BARROUX, and BRUNO DENIS. *Bull. mem. l'ecole prep. med. pharm. Dakar*, 1953, 1: 43.

THE AUTHORS discuss a group of cases in which thrombosis had occurred within the cardiac chambers as an acute complication of various surgical procedures. The report originates from Western Africa.

Anatomically, the thromboses are implanted upon the endocardium where the blood currents are less rapid than elsewhere. The thrombosis is often firmly adherent to the endocardium, but on occasion is dislodged and obstructs the pulmonary arterial pathway. It is evident from this study that the thrombotic process ordinarily affects the right heart, but rarely the left heart. The thrombotic phenomena are usually acute and the thrombi are either merely in contiguity with the endocardium in its early stages or are actually penetrated by inflammatory elements and fibrocytes in the more chronic ones. In late cases the endothelium of the endocardium may cover the thrombus.

It is interesting to note, with respect to the West African population, that the ordinary venous thrombosis in the lower extremities seems to be superseded by a form of cardiac endocardial thrombosis, for, in autopsy studies, peripheral venous thrombosis has been found to be uncommon in this region.

—*Orville F. Grimes, M.D.*

Hypothermia as an Adjuvant in Cardiovascular Surgery; Experimental and Clinical Observations. H. WILLIAM SCOTT, JR., HAROLD A. COLLINS, and JOHN H. FOSTER. *Am. Surgeon*, 1954, 20: 799.

IN EXPERIMENTAL work performed on adult mongrel dogs, hypothermia was induced by means of immersion in a tub of ice water until the animal's temperature had fallen to 29 degrees C. With the dog anesthetized and cooled, procedures were carried out on the heart during varying periods of inflow stasis, outflow stasis, and combined inflow-outflow stasis. The results obtained indicate that hypothermia improves the survival rate.

Hyperventilation during cooling and operation also had a favorable effect on the survival rate. The combination of inflow and outflow stasis was tolerated well by the hypothermic dog's heart for only 5 to 6 minutes.

In a series of 11 patients, the immersion method of cooling proved to be quite satisfactory. In infants and young children, only 12 to 30 minutes in ice water, after induction of anesthesia, were required for reduction of body temperature to the desired range. In the one adult subjected to the immersion technique, a period of 48 minutes was required to reduce the temperature to 30 degrees C., with a further drop to 28 degrees C. after the patient had been removed from the ice water. It is interesting to note that in 7 cyanotic infants the cyanosis disappeared during hypothermia.

On the basis of these experimental and clinical observations it appears that hypothermia is a real aid in cardiovascular surgery.

—*Benjamin F. Lounsbury, M.D.*

Experimental and Clinical Observations on the Closure of Cardiac Septal Defects. HARRIS B. SHUMACKER, JR. *Angiology*, 1954, 5: 289.

THE AUTHOR and his associates produced (in dogs) large atrial septal defects which tended to remain widely patent over long periods of time and which were strikingly like those encountered in patients. Successful surgical closure was effected repeatedly and without mortality by suturing to an incision in the right atrial wall roughly parallel to the interatrial groove a half moon-shaped pocket of autogenous pericardium which could then be invaginated into the atrial cavity. The posterior wall of the pocket could be pushed against the septum so as to permit clear palpation of the defect and careful suturing of the pericardium to the rim of the defect. The grafts survived and remained firmly united to the septum. This operation as finally developed was used in 2 severely ill children who tolerated the procedure well. One showed gratifying clinical improvement; the other died 5 months after operation, and, in contrast to the results in dogs, postmortem examination showed the pericardial graft to have disappeared, presumably because of failure of sufficiently rapid vascularization.

Modification of the method, simply by substituting pockets made of thinly woven nylon for pericardial grafts, was tested in dogs. It was found that the plastic material quickly became covered with endothelium and firmly incorporated with the septal wall. The method was employed in the case of an 11 year old

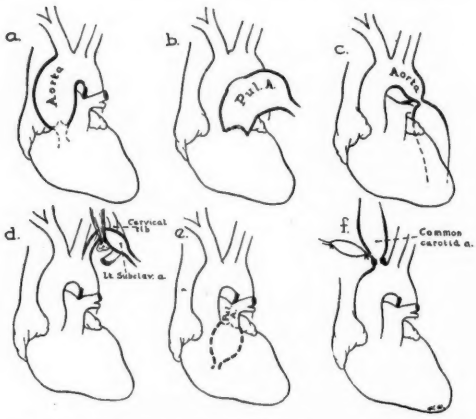


FIG. 1 (Holman). Types of poststenotic dilatation. Poststenotic dilatation is most pronounced beyond a subaortic stenosis, equally prominent beyond a pulmonic stenosis, less developed beyond a coarctation of the aorta, mildly present distal to compression of the subclavian artery between the scalenus anticus muscle and its attachment to a cervical rib, occasionally present in the small ampulla between an infundibular stenosis and the pulmonic valve, and in a unique instance it occurred distal to a partially occluding band applied to the innominate artery. The degree of poststenotic dilatation is intimately dependent upon height of pressure and upon velocity of flow.

boy who tolerated closure of his septal defect so well it was possible to proceed with pulmonary valvulotomy at the same operation. The overall result was excellent.

The author next gave his attention (experimentally) to large defects of the ventricular septum. The method evolved to close them successfully entailed the passage of a tubular graft by means of a blunt tipped needle through the septum and through the midportion of the defect so that the tube when distended would obturate the opening between the ventricles. A finger inserted through a small incision in the left ventricular wall was used for palpation of the defect and guidance of the graft. The tubular graft of pericardium was so constructed that that part lying in the defect would balloon out when blood was injected into it through a removable small plastic tubing. The injected blood eventually became organized with fibrous tissue and the surface became endothelialized. Animals in a state of severe cardiac failure stood the procedure very well and were promptly relieved of all cardiac dysfunction.

Experiences with this operation in 5 critically ill children are detailed. Whereas but 1 child survived and is markedly improved, the operation nevertheless appears to offer promise of solution of a difficult technical problem, and it is hoped that further experience with this procedure and modifications of it may render it safer and more uniformly successful.

—*Edwin J. Pulaski, M.D.*

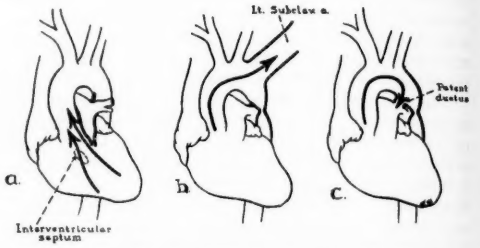


FIG. 2. Conditions preventing poststenotic dilatation. Certain conditions prevent dilatation beyond a stenosis: (a) an interventricular septal defect and an overriding aorta provide diversion of blood away from the pulmonary artery, thus diminishing pressure and velocity of flow through the accompanying infundibular stenosis (tetralogy of Fallot); (b) a large subclavian artery may divert a large volume of blood away from a coarctation, thus preventing dilatation beyond the coarctation; (c) a large open ductus proximal to a coarctation effectively diverts a volume of blood away from the coarctation sufficient to prevent dilatation of the aorta beyond the coarctation.

The Obscure Physiology of Poststenotic Dilatation; Its Relation to the Development of Aneurysms. EMILE HOLMAN. *J. Thorac. Surg.*, 1954, 28: 109.

AN EXCELLENT PRESENTATION of the explanation of poststenotic dilatation and its relationship to the development of aneurysms is presented. This phenomenon has been observed many times by surgeons, but an adequate reason for its presence and an explanation of its mechanism have never been adequately presented. Several very interesting experiments were performed and an analysis of the findings was presented.

It was found that a mass of fluid ejected through a narrow and limited constriction under high velocity strikes against a more slowly moving mass of fluid distal to the stenosis, which results (1) in the conversion of high kinetic energy into high potential energy or lateral pressure, and (2) in the lateral deflection of the rapid stream and even in a complete reversal in its direction of flow, the resulting clash of opposing streams producing eddies of alternating high and low pressures which through repeated impacts over a long period of time against an elastic wall are capable of inducing structural fatigue and distention of that wall. The accentuating play of these forces is another factor. The hydraulic principle is that a widening stream causes decreasing velocity, which in turn produces increasing lateral pressure. Thus, the interplay of these three factors recurring repetitively with each systole in a pulsating stream and operating in a limited segment of an elastic vessel will eventually and inevitably produce the phenomenon of poststenotic dilatation. This sequence of events may be the initiating and possibly the most important factor in the development of fusiform dilatations, saccular aneurysms, or even of the dissecting aneurysms commonly observed in the arteriosclerotic aorta in which segmental atherosclerosis or fibrosis may produce a localized or a relative stenosis.

The recognition of the potential power of the hydraulic forces which are liberated beyond a real or a relative stenosis may exist in the explanation of the destruction of bone and surrounding structures that occasionally accompanies the development of a thoracic aneurysm. These forces may also explain the aneurysmal dilatation of the vein usually seen at the site of an arteriovenous fistula where the arterial stream under high pressure and high velocity is ejected through an abnormal communication into the widened bed of the accompanying vein.

The aneurysmal dilatation of the pulmonary artery in the presence of a patent ductus may also be ascribed to the hydraulic forces liberated when the arterial stream of high pressure and high velocity is ejected from the narrow ductus into the wider and less rapidly flowing stream of the pulmonary artery with its lower pressure. It has been pointed out that it is probable that the sudden cerebral hemorrhage attributed to the rupture of a small aneurysmal dilatation has its inception in the precipitate unleashing of hydraulic forces suddenly augmented by the heightened pressure and increased velocity of flow incident to emotional stress or physical exertion. Sudden death from the rupture of a larger thoracic or abdominal aneurysm may follow the sudden increase in blood pressure and pulse rate that accompanies emotional stress or physical exertion and produce an increase in the velocity of flow which greatly augments the play of hydraulic forces with resulting sudden increase in lateral pressure just distal to the junction of the narrow arterial lumen with the greatly widened bed of the aneurysmal dilatation.

It has been pointed out by the author that in vascular surgery, methods of end-to-end anastomosis must be done with the thought that the anastomosis should be performed in order to allow for the growth at the site of the union as the child grows, in order that future stenosis will not occur. Also, methods should be followed which will prevent or minimize the development of constriction at the site of anastomosis, either by puckering at the time of operation or by cicatricial contracture as healing progresses.

—*John E. Karabin, M.D.*

Natural History of Aneurysms of the Aorta. JOHN J. CRANLEY, LOUIS G. HERRMANN and ROSAMUNDE M. PREUNINGER. *Arch. Surg.*, 1954, 69: 185.

SURGEONS have demonstrated during the past few years that excision of an aortic aneurysm is feasible with restoration of the continuity of the aorta in man by means of an arterial homograft of considerable length. The immediate benefits from this operation are striking; however, long-term observations are not available.

Controlled studies on the clinical course of aortic aneurysms have not been reported because of the low incidence of the condition and failure to reveal asymptomatic and nonfatal aneurysms of the aorta.

In order to eliminate some of the many variables, the present study is limited to aneurysms of the aorta which were studied at autopsy. The autopsy protocols and clinical records of all patients at the Cincinnati General Hospital with a pathologic diagnosis of aneurysms of the aorta, between the years 1926 and 1952 inclusive, were reviewed. There were 103 dissecting aneurysms; these were excluded from the study. A saccular or fusiform aneurysm was found in 243 subjects among 17,168 autopsies, an incidence of 1.4 per cent.

It was possible to determine the etiology of the aneurysm in 230 subjects; of these, 180 (82.0%) were syphilitic, 32 (14%) were arteriosclerotic, 3 (1.3%) were syphilitic and arteriosclerotic, 5 (2.2%) were mycotic, and 1 (0.4%) was traumatic.

It was found that the aneurysm was the primary cause of death in 103 cases (45%); the major contributory cause in 23 (10%); the minor contributory cause in 13 (6%); and an incidental finding in 90 (39%). Group I is made up of cases in which aneurysms were the primary cause of death. Group II comprises those cases in which aneurysms were the greatest contributory cause, although not the sole or primary cause of death. This group includes those patients who died of pneumonia and who were found to have partial tracheal obstruction or extensive compression of the lung by the aneurysm. Group III is made up of instances in which the aneurysm was a contributory cause of death, but of less than major significance. Group IV includes those aneurysms considered to be incidental and having taken no part in the subject's death.

Most aneurysms in group IV were small, although some were large. Included in this group is one case in which the aneurysm filled the entire left hemithorax, but the patient died at the age of 83 from injuries sustained in an automobile accident. Also included are aneurysms described as "beginning." From the figures given it is calculated that 45 per cent of all aortic aneurysms in this series were fatal, and an additional 10 per cent were a major contributing factor to death.

The incidence of aortic aneurysm in this series of 17,168 autopsies, exclusive of dissecting aneurysm, of which there were 103, was 1.4 per cent. The average incidence of 1.5 per cent was found in 9 similar investigations in England and in the United States.

Fifty-two aneurysms were found in the ascending aorta, 28 in the ascending aorta and arch, 50 in the aortic arch, 22 in the arch and descending aorta, and 14 in the descending aorta. The sites given are for syphilitic aneurysms of the thoracic aorta.

In a total of 53 cases, the avenue of hemorrhage from ruptured syphilitic aneurysms was from the following organs and in the frequency indicated: esophagus, 12; pericardium, 8; pleural cavity, 8; lung, 7; trachea or major bronchi, 4; through the anterior chest wall, 2; into the pulmonary artery, 2; retroperitoneal space, 6; peritoneal cavity, 2; superior vena cava, 1; and mediastinum, 1. Of the 20 syphilitic abdominal aneurysms, 2 (10%) were located below the renal arteries and 18 (90%) were above these arteries.

The symptoms observed in fatal syphilitic thoracic aneurysms were: cough, dyspnea, pain, weight loss, hemoptysis, hoarseness, and hematemesis. The signs noted were tracheal tug and tracheal deviation.

Thirty-two aortic aneurysms resulted from arteriosclerosis, an incidence of one arteriosclerotic aortic aneurysm in 537 autopsies. The aneurysm caused death in 25 per cent of the cases but had no significant effect on the patient's life in 75 per cent of the cases,

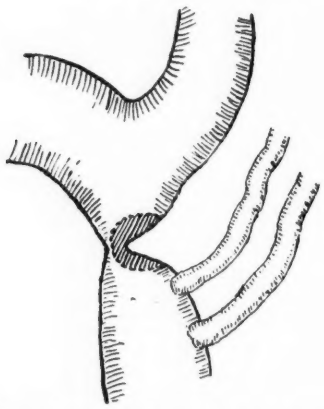


FIG. 1 (Walker, Haxton). Shaded area represents extent of excision when only a crescent is removed.

The arteriosclerotic aortic aneurysm was the primary cause of death in 8 cases, the major contributory cause in none, a minor contributory cause in 2, and an incidental finding in 22. The thoracic aorta was involved 12 times and the abdominal aorta, 20 times (all below the renal arteries).

In this study, 2 mycotic aneurysms and 1 traumatic fatal aneurysm are included. Twenty per cent of the syphilitic aneurysms and 27 per cent of the arteriosclerotic aneurysms were multiple. X-ray examination provided the most accurate means of confirming the diagnosis. Erosion of the vertebrae was found in 29 autopsies.

It is frequently supposed that rupture of an aneurysm causes sudden death but this is not always true. In 25 per cent of the instances of rupture of a syphilitic thoracic aneurysm, the patient lived over 6 hours following the rupture, and 15 per cent of these lived over 24 hours. Death appeared to occur more quickly after rupture of a syphilitic abdominal aneurysm. The prevention of death from rupture of an aneurysm might be possible if definitive surgical treatment can be instituted even in what now is considered the terminal episode. —*John H. Mohardt, M.D.*

The Surgical Treatment of Coarctation of the Aorta. R. MILNES WALKER and HERBERT HAXTON. *Brit. J. Surg.*, 1954, 42: 26.

THE EARLIEST possible repair of coarctation of the aorta, before damaging local and general changes occur, is recommended for all patients, unless in childhood there is only slight elevation of the brachial blood pressure. However, even in those cases, if the collateral circulation is inadequate to produce pulsations in the femoral vessels by the age of 14 or 15, surgery is recommended. The optimum ages for repair fall between 5 and 15 years. Beyond the age of 30 surgery is not advised.

In 27 cases a modification of the usual excision was employed. By taking advantage of the medial eccentric position of the aperture through the coarctation in the cases presenting a transverse lateral sulcus marking a short coarctation, a crescentic excision of the lateral part of the aorta, including the sulcus, is carried out (Fig. 1). This leaves a bridge of normal aorta across the anastomosis for greater strength and to promote growth.

In other cases complete resections and anastomoses were performed. In 2 cases, grafts were used.

The reported results were 2 operative deaths, and normal active life for the survivors (followed up to 6 years). Of interest are these special cases: a successful crescentic excision in a 10 month old infant; ligation of an abnormally placed right subclavian artery below the coarctation with return of the right radial pulse a few days after operation; bypass of a subcoarctation aneurysm with an iliac artery homograft with the aneurysm left in situ.

—*Leonard D. Rosenman, M.D.*

ESOPHAGUS AND MEDIASTINUM

Simple Stricture of Esophagus. E. C. MEKIE. *Brit. J. Surg.*, 1954, 42: 39.

THE HIGH incidence in Malaya of long strictures of the esophagus following accidental ingestion of caustic soda has stimulated the author to adopt a modification of Allison's procedure for esophageal carcinoma, in 10 cases of stricture. Certain technical problems arise because of the high level at which the by-pass must be connected. A long Roux-type loop of jejunum is prepared, passed up into the chest, and sutured side-to-side to the esophagus above the aortic arch. The spleen is removed as the initial maneuver to provide easy passage of the loop through the diaphragm. The long loop is prepared by dividing the jejunum and its mesentery just below the level of the second intestinal artery, dividing the next 3 arteries as they arise from the superior mesenteric vessel, and slitting the mesentery between those arteries toward the first arcade, which is preserved with great care. The limiting factor in achieving adequate lengths of jejunum is the length to which the mesentery can be stretched without impairing flow through its vessels. In 4 cases atypical vascular patterns interfered with the usual method of construction of loops.

The loop is passed through the mesocolon, and through an opening in the diaphragm midway between the tip of the ninth rib and the esophageal hiatus. It may be very difficult to expose enough esophagus in the posterior mediastinal apex, behind the left subclavian artery. Usually only a single layer anastomosis (linen) has been feasible.

The abdominal dissection is performed through a ninth rib thoracoabdominal incision; a fifth rib thoracotomy is used for the latter part.

The stricture-bearing esophagus is not resected. Cyst formation, as reported by Deaton and Bradshaw, has not been observed.

The results in 10 cases are as follows: attempts in 2 cases were abandoned because of failure to free the esophagus; attempt was abandoned in 1 case when defective vascular arcades caused failure of the loop; death occurred in 2 cases; and satisfactory results were obtained in 5 cases (4 years, 3 years, 2 years, 6 months, and 4 months after operation).

—*Leonard D. Rosenman, M.D.*

Abnormal Ring Contractions of the Thoracic Esophagus; with an Account of Familial Manifestations. T. V. L. CRICHLOW and H. J. SHAW. *Brit. J. Surg.*, 1954, 42: 46.

A PHENOMENON of multiple segmental spasms of the circular smooth muscle in the lower two-thirds of the esophagus has been observed. The radiologic appearance has variously been termed curling, corkscrew esophagus, tertiary contractions, ripple esophagus, and *spasmes à etages* (Barsony-Teschendorf syndrome). The effect on the patient, usually an elderly male, is variable, causing no complaints in some cases, and mild or severe dysphagia or regurgitation in others. The contraction rings tend to become persistent, and may cause cardiac obstructions. Associated cardiospasm, diverticula, and hiatus hernias may be observed, as well as carcinomas and peptic ulcers. Indeed, chronic esophagitis may account for some of the symptoms.

Patients have been relieved by a variety of drugs, including atropine, nitrites, amphetamines, pentamethonium and curare.

An unusual familial pattern is reported here. Six out of 8 siblings were noted to demonstrate the abnormal contractions. In 2 of these, the eldest brothers, symptoms occurred. In one, bouginage and antispasmodic drugs gave relief; not so in the other brother, who has been referred for surgical correction of cardiospasm. —*Leonard D. Rosenman, M.D.*

Esophageal Hiatus Hernia; a Clinical Study Based on 138 Cases, of Which 96 Were Treated Surgically. DOUGLAS ROBB. *Austral. N. Zealand J. Surg.*, 1954, 24: 18.

THE AUTHOR presents his experience in 138 cases of hiatus hernia. Ninety-six of the patients were treated surgically. The anatomy and physiology of these hernias are reviewed and the author stresses the fact that the division of these hernias into the various types that we know is purely an academic feature, as repair is essentially the same in all cases except those with a short esophagus. The latter type was extremely rare in his series.

Six patients in this series were infants or juveniles. This article does not deal with hernias of a congenital type which are usually at the left posterior diaphragm, but strictly with hiatus hernias. In these cases the confusing picture which usually arises might suggest first, a pyloric stenosis, or some stenotic lesion to produce the vomiting that is seen at any time after a few days to years after birth. The ill effects of such a hiatus hernia—acid esophagitis, bleeding, stricture, and ulceration—tend to develop promptly and can progress with alarming rapidity. The author suggests that the possibility of congenital hiatus hernia be borne in mind in the presence of vomiting and hematemesis in infants and young children. Confirmation by roentgenology and esophagoscopy should be sought, and surgical repair attempted once the diagnosis of the hernia is made, in the hope of forestalling the pitiful complications and sequelae, such as hemorrhage and esophagitis, ulceration and stricture. Once the latter two complications arise the possibility of restoration of the upper esophagus and lower esophagus to a normal functional tissue is very doubtful.

The operation routinely followed by this author is similar to that described by Richard Sweet. An incision is made in the ninth or tenth right rib cage with or without a rib resection. In 21 cases a counter-incision in the diaphragm was made in order to facilitate reduction of the hernia into the abdomen. In one of these instances a postoperative hernia through this counter-incision occurred. Only 4 of the hernias were repaired from the abdominal side, but in all cases a good reason was had for this approach.

Two of the 68 patients operated upon who were adequately followed up, died. One patient died of pulmonary embolism after he returned to his home, and another from a defect in the anesthetic equipment at the time of the operation. The hernia recurred in 11 of the 63 patients who were followed. Many of these patients, although showing recurrences, did not seem to have symptoms that were bothersome enough to warrant a reoperation. —*Matthew H. Evoy, M.D.*

Subtotal Esophagectomy for Bleeding Esophageal Varices. DENTON A. COOLEY and MICHAEL E. DEBAKEY. *Arch. Surg.*, 1954, 68: 854.

A NUMBER of methods has been employed to control bleeding from the esophagogastric region. Among indirect approaches to the problem are those which reduce the volume of the portal venous circulation, increase portal systemic venous communications, and reduce intrahepatic venous obstruction primarily by hepatic artery ligation; and finally, those which reduce peptic ulceration of the terminal esophageal mucosa. Direct measures aim to eliminate the source of bleeding by obliteration of the varices or by their surgical extirpation. None of these, however, has provided uniformly satisfactory results, and the authors therefore propose still another method consisting of extensive subtotal esophagectomy. The rationale of this procedure lies primarily in the more complete extirpation of the main source of hemorrhage.

For a number of reasons the region of the esophagus between the diaphragm and the azygos-vena cava junction may be regarded as the critical zone for esophagogastrostomy in the presence of portal hypertension. Admittedly, removal of this segment of esophagus may not influence the underlying condition causing venous collateral pathways, namely, portal hypertension. However, transplantation of the stomach to higher levels may provide opportunity for more direct drainage of portal blood into the azygos system and may minimize the tendency for recurrence of varices. In addition, by placing the anastomosis well above the diaphragm, wide excursions in intrathoracic pressure upon the esophageal venous bed are minimized. A further advantage lies in the reduced tendency for esophagitis to occur.

Exploratory laparotomy is performed, the spleen is removed, and the stomach is mobilized for transplantation into the thorax, care being used to preserve the right gastric and gastroepiploic vessels. Pyloromyotomy of the Fredet-Ramstedt type is routinely added to prevent troublesome gastric retention. A curved right submammary incision is then made and the chest is entered through the fourth intercostal space, the fourth costal cartilage being divided near the sternum. The esophagus is mobilized and the distal

two-thirds is withdrawn from the superior mediastinum, leaving the azygos vein intact. The stomach is advanced through the esophageal hiatus, the latter having been stretched bimanually. An anastomosis is then performed between the upper esophageal segment (more than 2 cm. above the level of the azygos vein) and a site on the anterior surface of the fundus of the stomach.

Experience with 3 cases of bleeding esophageal varices treated in this manner suggests that the procedure is applicable primarily to patients with bleeding esophageal varices having relatively little impairment of hepatic function. —*David H. Lynn, M.D.*

Mesothelial Cysts in the Posterior Mediastinum (Cisti mesoteliale a sede mediastinica posteriore). GIOVANNI ROLLO. *Ann. ital. chir.*, 1954, 31: 300.

THE AUTHOR reviews the literature, and presents a surgically proved case of a mesothelial cyst of the posterior mediastinum. The patient was a 22 year old carpenter who had had undiagnosed vague abdominal complaints for approximately 2 years. On a routine chest roentgenogram, a round opacity was seen in the region of the right diaphragm. Clinically, the patient was asymptomatic except for a chronic cough which was attributed to excessive smoking, and on physical examination of the chest no abnormalities were observed. Stratographic studies on the chest revealed the presence of an abnormal cystic formation in the right posterior mediastinum immediately above the right diaphragm.

Under general anesthesia, a thoracotomy was done with resection of the sixth rib, and the cyst was resected from the inferior visceral pleural surface of the right lower lung and the superior parietal pleural surface of the diaphragm. The tumor mass measured the size of an orange and contained clear fluid. On histologic examination, it was composed of a fibrocollagenous membrane which was epithelialized in small rare islands with cuboidal epithelium. This confirmed the diagnosis of mesothelial cyst. The patient made an uneventful recovery.

Since first described in 1854, by Duvernios, this entity has appeared sporadically in the medical literature. It has been given numerous names, but they all appear to be of mesothelial origin. As with other cystic formations in the body, they can give rise to complications such as inflammation, perforation, hemorrhage, and malignant degeneration. The most frequent complication observed is that of inflammation. Except in the presence of complications, these cysts are usually clinically asymptomatic.

These cysts are considered by some to be a herniation of the pericardial serosal membrane in between the pleural reflection of the lung. Others consider them to be due to lymphatic obstruction. The author is of the opinion that they are congenital in origin, being due to a coalescence of the primitive mesenchymal lacunae.

These lesions are usually well demonstrated by stratigraphic studies. Transthoracic puncture for diagnosis or treatment is contraindicated, and the only successful treatment consists of surgical resection of the mesothelial cystic formation.

—*Roland A. Manfredi, M.D.*

MISCELLANEOUS

Therapy of Myasthenia Gravis; Indications and Limitations of Thymectomy (Possibilità attuali nella terapia della miastenia gravis, indicazioni e limiti della timectomia). G. BOCCHETTI and A. LUCIFERO. *Arch. ital. chir.*, 1954, 77: 337.

THE EVOLUTION of the pathologic changes in myasthenia gravis has centered about three basic mechanisms. The neurogenic theory has been discarded because of the repeated difficulty in attempting to demonstrate lesions in the central and peripheral nervous system. The consistent finding of atrophic degeneration, lymphorrhagia, and plasma cell infiltrations in the striated muscles have given added support to the myogenic origin of myasthenia gravis. These lesions have also been found in the cardiac muscle, liver, pancreas, adrenals, brain, and spinal ganglia. More recently, the endocrine alterations in this disease have received added attention. Myasthenic symptoms have been seen in hyperthyroidism, adrenal insufficiency, castration, and in cases of adenoma of the adrenals and the thymus gland. It has also been demonstrated that pituitrin has the property of transmitting impulses at the myoneural juncture.

The incidence of myasthenia gravis is increased between the second and third decades. Under 40 years of age, there is an increased incidence in women. Familial and hereditary factors are not consistent enough for conclusions. The first muscles involved are usually the extrinsic muscles of the eye, and the muscles of mastication, deglutition, and phonation. This is followed by involvement of the facial and respiratory musculature. The muscles of the extremities are only mildly involved, and there is a characteristic improvement in function following rest, with an accentuation of symptoms on fatigue. Although interrupted by periods of improvement, the course of the disease is usually progressive and fatal; however, temporary remissions and spontaneous cures have been reported.

There are three current theories regarding the delayed transmission of the nerve impulse at the myoneural juncture in myasthenia gravis. The similarity between a myasthenic patient and a normal patient under the influence of curare has led some authors to affirm that they have isolated a curarelike substance in the peripheral blood of patients with myasthenia gravis (Walker, Korpassy). Pharmacologic studies have shown that acetylcholine is necessary for the electrical depolarization at the myoneural juncture. Still other investigators, with the use of prostigmine, have demonstrated an excess of cholinesterase activity at the myoneural juncture in myasthenia gravis.

The diagnosis of myasthenia gravis can usually be made by demonstrating a rapid diminution in the contraction following faradic stimulation; progressive increase in electrical amplitude required for muscular contraction; hypersensitivity to intravenously administered curare; aggravation following the administration of quinine and improvement with prostigmine; and the demonstration of a 15 per cent enlargement of the thymus.

The endocrine disorders seen in this disease have prompted investigators to perform such procedures as

carotid sinus denervation and resection of the adrenal cortex. No consistent results have been obtained from these procedures. Following the first thymectomy for myasthenia gravis by Sauerbruch, in 1912, there have been increasing reports of good results from this procedure. A collected series of positive reports reveals that 35.5 to 77 per cent of the cases show some definite signs of improvement postoperatively.

The authors report 3 cases of myasthenia gravis, in which a thymectomy was performed.

The first case is that of a 54 year old male who had a gradual onset of ophthalmoplegia, ptosis, and bulbar paresis over a period of 6 months. Laminagraphs of the chest demonstrated an enlarged thymus gland. The patient received a course of roentgen therapy to the thymus with no improvement. At operation a small apple-sized thymus gland was removed. The patient received prostigmine during the postoperative course, and made an uneventful recovery. Four months after surgery the patient had returned to his normal activities, requiring only one and one-half tablets of prostigmine per day. Formerly, this patient had taken up to six tablets of prostigmine with very little relief of symptoms.

The second case is that of a 23 year old male who had myasthenia gravis affecting the pharynx, larynx, and the upper extremities for 3 months. Anterior pneumomediastinal planograms did not demonstrate any abnormality of the thymus. The symptoms were poorly controlled with 8 tablets of prostigmine per day. A thoracotomy was performed and the thymus was removed. Immediately after operation the symptoms were well controlled with two tablets of prostigmine per day for 2 months; but after an interval of 6 months the patient required up to 8 tablets of prostigmine. The pathologic examination of the resected tissue showed a normal glandular architecture with hyperplastic activity.

The last case is that of a 61 year old woman who had a 2 year history of ocular and bulbar myasthenia gravis. This patient had a basal metabolic rate of +37.7, and had formerly been treated for a neuropsychiatric disturbance. A pneumomediastinal laminagraph revealed an enlarged thymus. A thymectomy was done under general anesthesia, but the patient died on the second postoperative day of respiratory paralysis.

The authors recommend thymectomy in myasthenia gravis when there is demonstrable evidence of enlargement. The procedure should be done early in the disease process, and is more definitely indicated in the younger age group.

In the absence of thymic enlargement, the authors advocate thymectomy in those cases that do not respond to medical management.

—*Roland A. Manfredi, M.D.*

SURGERY OF THE ABDOMEN

GASTROINTESTINAL TRACT

Experiences with Upper Gastrectomy: Its Relationship to Esophagitis, with Special Reference to the Esophagogastric Junction and Diaphragm; a Study in the Dog. ELVIN W. HOAG, LAWRENCE B. KIRILUK, and K. ALVIN MERENDINO. *Am. J. Surg.*, 1954, 88: 44.

THIS experimental study is concerned with the relationship of upper gastrectomy to esophagitis. All of the experiments were done on dogs, with special reference to the esophagogastric sphincter.

Studies were first done to determine the actual weight and area measurements of the intact total stomach in an effort to determine percentile excision of the upper stomach.

In the first series of dogs (16) a proximal transection of the gastrointestinal tract was done below the esophagogastric border; a small rim of gastric wall was left, the vagus nerves were sectioned at this level, and a cardiogastrostomy was carried out below the diaphragm.

In the second group of animals (11) the procedure differed in that the vagus nerves were severed 2 to 4 cm. above the diaphragm, and the esophagus was transected above the gastric margin. Anastomosis was done below the diaphragm. Esophagoscopy, determination of the gastric secretory response to histamine, and autopsy studies were done as part of the study. Total, 75 per cent, and 50 per cent gastrectomies were performed in both series.

In the first group no esophagitis was observed on esophagoscopy, and only minimal questionable esophagitis was found in 1 animal at autopsy. In the second group, 9 of 10 animals showed the presence of either esophagitis or ulcer. In 2 of these dogs perforation of esophageal ulcers occurred on histamine injection.

The authors comment that these results substantiate the opinion of others that segmental resection of the stomach protects against histamine-induced gastric and duodenal ulcer in the dog and probably in the human being also. However, such procedures are inadequate in preventing esophagitis or esophageal ulcer if the esophagogastric ring is excised. The findings emphasize again the extreme sensitivity of the esophagus to chemical trauma. It would appear that in human beings, following sacrifice of the esophagogastric ring, only an occasional patient will escape esophagitis.

Inasmuch as an anastomosis was done below the diaphragm in both series of experiments the effect of the diaphragm is not a factor. The authors believe therefore that the presence of a "sphincter" is the only mechanism preventing gastric reflux and esophagitis. The results also indicate that in hiatal hernia it is necessary to replace the gastric pouch below the diaphragm. Another practical point is that in total gastrectomy for carcinoma a small rim of gastric wall should be left, if possible, for the anastomosis.

—Donald C. Geist, M.D.

Total Gastrectomy with Replacement Utilizing the Transverse Colon; Preliminary Report. DAVID H. WATKINS, GEORGE WITTENSTEIN, and JACK DANIEL. *Arch. Surg.*, 1954, 69: 167.

THE PRESENT report deals with the replacement of a totally gastrectomized stomach by a segment of transverse colon with its blood supply. The poor nutritional state of the patient after gastrectomy, digestive disturbances, rapid emptying, diarrhea, and steatorrhea are discussed.

It has been the belief of many observers that the most important contributing factor in this disability of totally gastrectomized patients is the absence of a mechanical reservoir. A short history of attempts to replace resected stomachs with intestinal or colonic segments is presented, and the advantages and disadvantages are described. Five cases in humans are reported in detail, with comment on each case.

The authors do not advocate total gastrectomy for benign gastric lesions or for malignant gastric lesions which can be adequately resected by subtotal gastrectomy. It is their opinion that proximal subtotal gastrectomy followed by esophagogastrostomy is inadequate for the treatment of juxtacardiac and cardiac lesions because of the occurrence of peptic esophagitis. The problem of the pathologic nature of any gastric ulcer is still existent and a definitive method of preoperative diagnosis is eagerly awaited.

In those cases in which it is believed that total gastrectomy is indicated, the transverse colon offers certain advantages as a replacement for the excised stomach and esophagus, especially in cases of carcinoma of the fundus and cardia. The transverse colon segment possesses excellent vascularization, and a sufficient length is obtainable so that it may be extended into the neck if required. The incision of choice for total gastrectomy, whether replacement is by the ileocolon or a segment of transverse colon, is a left thoracoabdominal incision with a transpleural, transdiaphragmatic, transabdominal approach.

Diarrhea has occurred in 4 of the 5 total gastrectomies reported, and the authors attribute the diarrhea to the associated complete vagotomy. Postprandial cramping, especially after the ingestion of large quantities of liquids, has been a constant feature regardless of whether the right ileocolon or the transverse colonic segment has been used for replacement. In the authors' cases, the cramping after meals consistently developed between the tenth and the thirteenth postoperative days. It has responded to the administration of antispasmodics, which were not required after several weeks.

The occasional regurgitation of food in various stages of digestion during the daytime and of small quantities of bile at night has been noted. Postmortem examination in one case and esophagoscopic examination in the others failed to visualize evidence of esophagitis.

Five cases are presented in which total gastrectomy was performed and restoration of continuity was ac-

complished by esophagojejunostomy, by transplantation of the ileocolon, and by the transplantation of a segment of the transverse colon. The salient features of these cases are compared and contrasted. Two surviving patients in whom the resected lesion was benign are available for long-term evaluation.

Segments of the transverse and left colon are admirably adapted anatomically to be used as replacements for the totally excised stomach and esophagus. They restore the "crop function" of the stomach. All types of implants of colonic segment are associated with certain transient postoperative disturbances, including mild regurgitation and esophageal reflux.

—*John H. Mohardt, M.D.*

Combined Abdominoperineal Herniorrhaphy for Massive Rectal Prolapse. EDWARD T. NEWELL, JR. *Ann. Surg.*, 1954, 139: 864.

A MASSIVE rectal prolapse is a progressive lesion; at first it occurs chiefly when straining at stool. As time goes on, any straining at work may cause the rectum to protrude. Strangulation of the rectum may occur if the prolapse is not reduced. The condition is in reality a type of abdominal hernia with weakness and separation of the transversalis fascia and elongation of the suspensory ligaments of the rectum.

In the past decade most surgeons approached the defect through an abdominal incision and by using some type of suspension of the sigmoid and rectum. The author uses the abdominal method of Pemberton and Stalker, combined with the perineal repair of Brintnall. The abdomen is opened through a lower midline incision. The sigmoid is pulled taut and an incision is made in the peritoneum on both sides of the mesentery and carried forward toward the bladder, meeting in the midline. The dissection is then carried down around the sigmoid and rectum. With the hand in the hollow of the sacrum, the rectum is freed further by blunt dissection down to the coccyx. The same procedure is carried out anteriorly between the bladder, prostate, and rectum. The rectum is elevated upward and fixed to the promontory of the sacrum and other portions of the pelvis. If this new position can be held for several weeks, the adhesions and scar tissue in the hollow of the sacrum should keep the rectum elevated permanently.

A successful case is appended.

—*Stephen A. Zieman, M.D.*

Duodenal Ulcer in Children; 2 Cases of Ulcer with Stenosis (L'ulcère du duodénum chez l'enfant a propos de deux cas d'ulcères sténosants). MARCEL MORIN, ALAIN MOUCHET, and MARTHE GAUTIER. *Arch. mal. app. digest.*, Par., 1954, 43: 481.

TWO CASES of obstructing duodenal ulcer in children are reported. One patient was a 14 year old girl and the other was a 16 year old boy. The symptoms of duodenal ulcer had been of 6 months' duration in the first case and of 3 months' duration in the second. The 2 cases had the following features in common: complete or almost complete pyloric obstruction, enormous gastric distention, and malnutrition. In 1 case the ulcer was on the anterior wall of the duodenum while in the other it was penetrating into the body of the pancreas. Both patients were treated by posterior gastroenterostomy, and in 1 of them a vagotomy was added. During follow-up periods of 2 and 5 months, respectively, both patients were completely rehabilitated.

Peptic ulcers occur more frequently in the newborn than in children in other age groups. Duodenal ulcers in children are twice as common as gastric ulcers. They affect boys and girls with equal frequency.

Perforation is the most common complication of peptic ulcer in the newborn. In older age groups obstruction is the most common complication, perforation being second, and hemorrhage third.

Treatment, as in the adult, is usually medical. When surgery is indicated, gastroenterostomy is preferable to gastric resection.

—*Frederick W. Preston, M.D.*

Colonic Resection for Diverticulitis. EDWARD WILSON. *Austral. N. Zealand J. Surg.*, 1954, 24: 36.

THE AUTHOR presents 15 cases of diverticulitis, which were encountered in his institution during the past 5 years. These patients were operated upon chiefly because of complications of the existing diagnosed diverticulitis. In 4 of the patients operation was required because of intestinal obstruction. In 3 patients a vesicocolic fistula was present, and in 8 patients resection was performed because of troublesome and intractable symptoms of diverticulitis without perforation or other complications. The oldest patient was 76 and the youngest was 34 years of age. In 11 of the 15 cases the rectosigmoid was resected and in 4 a left hemicolectomy was performed. Fourteen of the patients showed benign changes, whereas, in the remaining patient a malignancy of the sigmoid colon was found in conjunction with the inflammatory changes. There were no deaths or important complications following these operations, and all patients were discharged from the hospital apparently cured of their disease.

In each of 2 cases of hemicolectomy with prior colostomy, laparotomy revealed an inflammatory mass in the sigmoid colon and diverticulitis extending up to the descending colon. In each case the transverse and sigmoid colons were divided. A spur colostomy was formed and the two ends of the isolated left colon were brought to the surface. The colon was not removed at this stage because of the multiplicity of inflammatory adhesions. After a month the colostomy was closed and then subsequently the left hemicolectomy was performed.

The policy of performing a temporary colostomy above the inflamed bowel and subsequently restoring continuity over the diseased segment is apt to be followed by recurrent symptoms and he therefore advises against it. —*Matthew H. Evoy, M.D.*

Carcinoma of the Colon with Special Reference to Prevention of Recurrence. WARREN H. COLE, DOUGLAS PACKARD, and HARRY W. SOUTHWICK. *J. Am. M. Ass.*, 1954, 155: 1549.

THE RECURRENT invasion of carcinoma of the colon spreads by one or more of four different mechanisms: (1) lymphatic metastases, (2) extension by contiguity, (3) local implantation, and (4) venous metastases. It is the opinion of the authors that prophylactic meas-

ures can prevent these mechanisms of metastasis from occurring in the treatment of carcinoma of the colon by surgery. It is their belief that implantation of malignant cells into the suture line may take place, and malignant cell emboli to the liver can be produced at the time of operation unless certain precautions are taken. Local implantation at the anastomotic line, caused perhaps by dragging detached malignant cells with the suture line into the wall of the intestine where they survive and grow, is an explanation for one of the mechanisms of local recurrence at the suture line. To prevent this, ligation of the lumen of the colon several inches above and below the tumor is recommended before mobilization of the involved intestine is begun. When smears were taken from resected specimens between the ligature and the tumor, cancer cells were found. When smears were taken beyond the ligature, no cancer cells were found.

The second cause of metastasis—venous spread produced by the detachment of malignant cells from the venules and veins within the tumor during the mobilization of the specimen—can be prevented by ligating the vessels to be sacrificed before removing the tumor. Malignant cells can be found growing inside veins or in near the tumor, and were found in the saline solutions profused through the vessels of the tumor, which supported the contention that with the handling during mobilization of the tumor, cancer cells could be detached. Thus, the arteries and veins supplying the involved segment of colon should be ligated before the intestine is mobilized. The use of these procedures will frequently prevent metastases which otherwise might develop. With the addition of these two procedures, the results in the operative treatment of carcinoma of the colon should be improved. —*John E. Karabin, M.D.*

Cancer of the Large Bowel; a Follow-Up Study of 420 Cases from a Private, a Charity, and a Veterans Hospital. Duncan A. Cameron, Henry A. Chapnick, and Don W. McLean. *Arch. Surg.*, 1954, 69: 242.

The present report deals with the study of 420 consecutive, histologically proved cases of cancer of the large bowel in three large hospitals—Detroit Receiving Hospital, Grace Hospital, and Dearborn Veterans Hospital, Detroit, Michigan.

Two hundred and eighteen cases have been followed for 5 years. The ages of the patients varied from 14 years to 58 years. The locations of the lesions conformed to the generally known incidence of cancer of the large bowel. In the veterans' group, the greatest incidence was in the sixth decade; in the private group, the seventh decade; and in the charity group, the eighth decade.

As in other series, 8.1 per cent of the cancers occurred under the age of 40; 17 per cent of the patients in this group were over 70 years.

In the charity group 28 per cent were over 70 years and three-fourths of them (20) were admitted with acute abdominal involvement. Of these, 10 had obstructions and 5 had perforations and peritonitis. Very old patients appeared to be less sensitive and less alerted by the symptoms of serious disease.

In the charity group, 48 per cent had had symptoms for more than 1 year, 30 per cent had had symptoms for less than 3 months, and several had had symptoms for only a few days. Almost without exception these patients had not been examined digitally or sigmoidoscopically prior to admission, regardless of the duration of their symptoms. Over 40 per cent of their lesions could have been reached by such examinations. Sixty-six per cent had gross or occult blood in the stool, and one-third of the patients with lesions in the rectum and rectosigmoid had hemorrhoids. Two patients in this group had had hemorrhoidectomies in the recent past; 2 had undergone appendectomies during which cecal lesions were missed, and 4 had been subjected to exploratory laparotomies at which their lesions were not found.

The operative mortality in the private and charity groups varied from 20 to 25 per cent. In the veterans' group, the mortality was lower, since these patients were younger, and very few were admitted with obstruction and/or perforation.

In the private palliative group, when resection could be accomplished the operative mortality was only 13.3 per cent. When colostomy alone could be done the mortality rose to 70 per cent, and when only ileostomy could be done the mortality was 100 per cent. Of 26 patients who survived resection, three-fourths lived 6 to 24 months in relative comfort without local distress and annoyance of a colostomy.

The operative mortality in the three groups ranged from 8 per cent to 21 per cent. The mortality of 9.8 per cent in the private group is acceptable. The marked contrast between the veterans' and the charity groups reflects the selection of patients in each instance, as the surgical staff in the two hospitals is almost identical. The patients at the Charity Hospital were the aged and debilitated, with advanced disease. The veterans' group were younger, in better condition, and only a few required emergency surgery.

Two hundred and eighteen patients were followed for 5 years. In the private group 43.5 per cent, and in the charity group 35 per cent were presumably cured for 5 years, yet the 5 year survival rate in the two groups is practically the same. Of 89 patients who presumably were cured, only 33 (15.3%) were alive and well after 5 years. The 202 patients from the veterans' group do not show a better 5 year survival. Of 93 patients presumably cured, only 43, or 20 per cent of the total group, are now alive and apparently well.

Of the 218 consecutive admissions for cancer of the large bowel, 40 per cent of the patients were presumably cured when discharged; however, only 15.3 per cent were alive and well at the end of 5 years.

The results of this study indicate that of 100 admissions for cancer of the large bowel in the area studied, 40 per cent will leave the hospital cured, but only 15 per cent will be alive and well 5 years later.

—*John H. Mohardt, M.D.*

Significance of Reduction of the Intestinal Flora Prior to Operations on the Colon or Rectum. C. V. Munthe Fog. *Acta. chir. scand.*, 1954, 107: 291.

The author attempts to estimate the significance of the preoperative administration of various drugs in operations on the colon and rectum.

Formerly, primary resection of the colon was associated with a considerable mortality (25 to 30%), and

fecal contamination during the operation was believed to be the chief cause of leakage about sutures, and of peritonitis. To avoid this leakage, the Bloch-Miculicz method was devised, but could only be applied to certain cases. Another method of avoiding bacterial contamination was the so-called "closed anastomosis." A drop in mortality after operations on the colon was noted when slowly absorbable sulfonamides were used. Recently, antibiotics with wider spectra have been tested in this regard.

The author studied four groups of patients: one group in which no attempt was made to reduce the intestinal bacteria prior to the operation; another group in which the patients were treated preoperatively with phthalylsulfathiazole; a third group treated with terramycin plus streptomycin, or with chloromycetin, and finally a fourth group of patients who were treated with bacitracin plus neomycin.

The postoperative course in these four groups was compared. The material comprised 372 operations on the colon or rectum in patients seen from January 1, 1946 to January 3, 1953. In 216 cases the operations were abdominal perineal resections; in 75 cases, resections of the colon; in 34 cases, hemicolectomy; and in 47 cases low resection of the rectum. In judging the postoperative course, particular regard was paid to infectious complications that may have been due to fecal contamination.

Among 42 patients who had received no preoperative treatment, 6 had wound infections, 4 had diffuse peritonitis, and 9 died—2 of these from peritonitis. Among 112 patients treated with phthalylsulfathiazole, 17 had wound infections, and 8 patients had peritonitis. There were 10 deaths, 5 of these from peritonitis. The third group of 20 patients received preoperative treatment with terramycin and streptomycin. In 4 of these wound infections developed, but there were no instances of peritonitis. There were 3 deaths, none of which was due to infection. The last group comprised 21 patients who were treated with bacitracin plus neomycin, and in 1 of these wound infection developed. There were 2 deaths, neither of which was due to infection.

The author notes that these four groups of patients were not seen within the same period, and that the number of cases is not statistically significant. His conclusions are that reduction of the intestinal flora by means of bacitracin plus neomycin, prior to operations on the colon or rectum, give the best clinical results. These patients gave the impression of having a milder postoperative course with fewer infectious complications. —*Donald M. Clough, M.D.*

LIVER, GALLBLADDER, PANCREAS, AND SPLEEN

An Unusual Complication of Needle Biopsy of the Liver; Report of a Case. ALLAN A. KAPLAN, ALFRED FROBESE, and HENRY L. BOCKUS. *Gastroenterology*, 1954, 27: 227.

NEEDLE BIOPSY of the liver has an associated mortality rate of about 1 per cent. The morbidity rate is considerably higher. The principal complication of this procedure is hemorrhage, as the procedure is performed blindly and the liver is a very vascular organ. An occasional death due to bile peritonitis has been reported. In 1 case, perforation of he jejunum in a patient with carcinomatosis was responsible for the fatal outcome. In a few instances the needle has been reported to have passed through a thin right liver lobe and into an adjacent structure such as the portal vein. In the article being reviewed, the authors reported a case in which the biopsy needle passed through a tonguelike right lobe of the liver and lacerated the cystic artery. Massive intra-abdominal hemorrhage and shock ensued, which were finally controlled only by celiotomy, ligation and division of the cystic artery. and cholecystectomy. —*Harvey N. Lippman, M.D.*

The Management of Obstructive Jaundice in Infancy. E. M. GREANEY, W. H. SNYDER, JR., and LAWRENCE CHAFFIN. *Am. J. Surg.*, 1954, 88: 17.

THE authors review their experience with obstructive jaundice in infants during a period of 18 years at the Los Angeles Children's Hospital. Thirty-three infants with obstructive jaundice were explored during this time. One-third of these children had surgically remediable lesions, another third had normal extrahepatic biliary systems, and one-third had disease which was not surgically remediable. No race or sex predominance was noted. The average age was 3 months and the average duration of life was 10 months.

The common causes of obstructive jaundice in infants, in the order of probable frequency, are: atresia, inspissated plugs of mucus, choledochal cyst, enlarged lymph nodes, tumor, and cholelithiasis. A trial of magnesium sulfate and bile salts as advocated by Swenson and Fisher is an aid in diagnosis. Operative cholangiography is now routinely used.

Ten patients had normal extrahepatic duct systems. Seven of these are dead, and 3 are living and well. The latter are assumed to have had inspissated plugs of mucus as the cause of their obstruction.

The various anomalies of the bile ducts are illustrated. Nine patients had complete atresia of the biliary duct system. Anastomosis was done in 8 patients and 3 of these are living and well. In all 3 it was possible to anastomose the duct or gallbladder to the duodenum.

It is suggested that infants with steady, unremitting jaundice have a thorough diagnostic work-up and that exploration can be done as early as 4 weeks of age. Preoperative care includes antibiotics, blood, vitamin K, intragastric tube, and intravenous cutdown. The surgical technique consists of wide exposure through a transverse incision, cholangiography, and complete dissection of the portal triad before the case is given up. Early exploration is advocated.

—*Donald C. Geist, M.D.*

Experiments on Oxygen Saturation and Pressure in the Portal Vein After Ligation of the Hepatic Artery (Experimentelle Untersuchungen ueber O_2-Saettigung und Druck in der V. portae nach Ligatur der A. hepatica). EMIL BUECHERL and WALTER DUEBEN. *Langenbecks Arch. u. Deut. Zschr. Chir.*, 1954, 278: 239.

ACCIDENTAL or experimental ligation of the hepatic artery leads to fatal necrosis of the liver, whereas shunting of the portal vein blood into the vena cava (Eck's fistula) does not cause liver disturbances although 75 per cent of the blood circulating through

the liver stems from the portal vein and only 25 per cent from the hepatic artery.

The authors, of the Surgical Department of the University of Goettingen, Germany, performed experiments on dogs to study the question whether the loss of oxygenated blood after ligation of the hepatic artery can be compensated for via the portal vein.

In a series of 17 dogs the hepatic artery was ligated. Three dogs did not receive antibiotics postoperatively, and these animals died; the other 14 animals survived, under the protection of streptomycin and penicillin therapy. This confirms the observation made by other workers—that anaerobic bacteria are normally present in the liver and cause fatal necrosis if the blood supply is reduced, unless they are kept in check by antibiotics.

Eight to 9 months after ligation of the hepatic artery the main experiment was performed:

A tube was inserted in the right femoral artery and connected with a Statham pressure receptor; a polyethylene tube was introduced into the inferior vena cava via the right femoral vein. After laparotomy, a third tube was inserted in the portal vein via a mesenteric vein and connected with another pressure receptor. Two blood specimens were taken from each of the three tubes—one before and one 10 minutes after enough blood was withdrawn by venesection to lower the blood pressure to 50 to 70 mm. Hg. The oxygen saturation was determined in each of the specimens. Finally, arteriograms were taken to visualize the blood circulation in the liver of the animals operated upon.

The following results were obtained: the pressure and oxygen saturation were the same in the animals operated upon as in normal animals. After the bloodletting, the drop of blood pressure in the portal vein was equal in the animals operated upon and in the controls. The decrease of oxygen saturation was less marked in the animals operated upon than in the normal dogs. The arteriograms revealed that in the dogs operated upon, small arteries of various caliber had formed around the liver hilus during the interval following the ligation of the hepatic artery, and only in rare cases did the lumen of the newly formed vessels reach half the normal size of the hepatic artery.

—Werner M. Solmitz, M.D.

The Role of Intestinal Bacteria in Liver Necrosis Following Experimental Excision of the Hepatic Arterial Supply. WILLIAM E. SCHATTEN. *Surgery*, 1954, 36: 256.

EXCISION of the arterial supply to the liver in dogs results in death due to liver necrosis. In normal healthy dogs there is a continual seeding of the liver by bacteria that pass from the gastrointestinal tract to the liver via the portal vein. It is these pathogenic organisms that are responsible for the overwhelming infection and subsequent death that occurs following hepatic artery ligation. The Clostridium welchii, which is present in the livers of some healthy dogs, is a saprophyte and plays no role in the hepatic necrosis and subsequent death. It was demonstrated that infection is the decisive factor in determining necrosis following deprivation of the arterial blood supply, and gram-positive cocci are the most important of the organisms that invade the ischemic liver. The administration of antibiotics prior to hepatic artery ligation causes a marked decrease in the mortality rate.

The author excised the hepatic arterial supply in 45 dogs. Twenty-five were treated with orally administered neomycin and 20 were given no antibiotic therapy. The mortality rate of the neomycin-treated dogs was 28 per cent, whereas that of the control group was 90 per cent. Since neomycin is poorly absorbed from the gastrointestinal tract and therefore has little, if any, systemic effect, the mechanism of protection is postulated to be sterilization of the intestinal tract prior to operation.

The author believes these findings support the concept of the passage of bacteria from the intestinal tract to the liver via the portal vein in man, and therefore he suggests that sterilization of the gastrointestinal tract in all cases of hepatitis, regardless of the cause, be done.

—Ely Elliott Lazarus, M.D.

Primary Carcinoma of the Liver. J. A. COLEMAN, R. D. HAINES, and CHARLES PHILLIPS. *Gastroenterology*, 1954, 27: 166.

THE AUTHORS reviewed a series of 23 cases of primary carcinoma of the liver observed at the Scott and White Memorial Hospitals and the Santa Fe Hospital in Temple, Texas, from January, 1933 through December, 1953. The series included 21 primary liver cell carcinomas, 1 cholangioma, and 1 tumor of mixed type. All age groups were represented and the males outnumbered the females 18 to 5. Although 19 patients sought medical advice within 6 months after onset of the symptoms, only 4 were alive 8 months after the symptoms began. The diagnosis was proved by exploratory celiotomy and biopsy in 15 instances, at autopsy in 7 instances, and by the use of the Silverman needle punch biopsy in a single-case. Twenty-two of the 23 patients were of Caucasian ancestry; 1 patient was a Negro. The greatest incidence of cases occurred during the fifth and sixth decades with extremes of 2 years and 81 years.

While the clinical picture of primary carcinoma of the liver is variable and the diagnosis is rarely made preoperatively or ante mortem, the disease should be suspected in patients with weight loss, weakness, fever, abdominal pain, and hepatomegaly. Laboratory tests, singly or in combination, are disappointing. The presence of intrahepatic calcification, and bulging and elevation of the right hemidiaphragm on roentgenographic examination may be of diagnostic help. Carcinoma of the liver has 2 unusual pathologic characteristics: (1) a tendency to metastasize to the skeleton without other organ metastases, and (2) a tendency to invade abdominal venous channels. Its behavior in this respect is similar to hypernephroma.

Although carcinoma of the liver occurs more frequently in individuals over 40 years of age, its occurrence in infancy and childhood is well known. In 1938, Steiner reviewed 75 collected cases of primary carcinoma of the liver in childhood and added 2 cases of his own. About one-half of this group occurred in patients under 2 years of age, and one-third in infants under 1 year. The youngest recorded patient was reported by Wilbur, *et al.*, a 3 day old infant with skeletal

metastases. About 2 of every 3 cases reported in children occurred in males.

The relationship between primary carcinoma of the liver and cirrhosis has been well documented. In the series reported by the authors, this relationship was established in only 7 instances, an incidence of 30.4 per cent, which is well below the usual figure cited.

The prognosis in primary carcinoma of the liver is extremely poor. Eighteen of the 23 patients whose cases were reported died within 8 months after the onset of symptoms. Two patients, however, had symptoms for 20 months or longer prior to the establishment of the diagnosis; 1 patient lived 6 months and another 42 months following diagnosis without surgical treatment.

Surgical extirpation is the only therapeutic approach to this disease. Partial hepatectomy or lobectomy has been recorded 233 times in the literature to date. Survival for more than 5 years postoperatively has been reported, though rarely.

—Harvey N. Lippman, M.D.

Postcholecystectomy Amputation Neuroma. ROBERT H. HUME and ROBERT W. BUXTON. *Am. Surgeon*, 1954, 20: 698.

THERE is no doubt that one of the most common causes of persisting or recurring symptoms after cholecystectomy is the presence of a stone or stones in the bile ducts. Other possible causes of postcholecystectomy symptoms are hypertonicity of the ampulla of Vater, fibrosis of the sphincter of Oddi, surgical trauma to one of the bile ducts, the presence of an unnoticed malignant tumor, of low grade cholangiitis, and of a cystic duct stump.

Because of the abundant nerve supply to the biliary tree, both sympathetic and parasympathetic, it seems logical that some abnormality of nerve regeneration might in some instances occur after surgery in this area. In recent literature, 7 cases are recorded in which postcholecystectomy neuromas were found and removed at a second operation.

In the present report, 9 new cases are presented with this finding. In 7 of these the cystic duct stump was found to be hard and fibrous, and it was excised. Each of these contained an amputation neuroma. All 7 patients were asymptomatic for follow-up periods of up to 7 years.

In 2 patients, common duct strictures were found and a microscopic study of each excised duct segment revealed a neuroma. One patient was relieved of his symptoms and the other was improved.

This entity should be kept in mind as a possible cause of postcholecystectomy symptoms. The usual indication for surgery will be the suspicion of a common duct stone, and, whether the latter is found or not, a search should be made for a neuroma. Finding a neuroma should not deter the surgeon from his exploration of the common duct.

—Stanley W. Tuell, M.D.

Ductal Changes in Chronic Pancreatitis. JAMES J. BERENS, ARCHIE H. BAGGENSTOSS, and HOWARD K. GRAY. *Arch. Surg.*, 1954, 68: 723.

INASMUCH as experimental studies have emphasized the importance of ductal obstruction in the pathogenesis of chronic pancreatitis, the authors were of the opinion that a thorough study of the incidence and extent of dilatation of the pancreatic ducts would be of value in determining the type of surgical procedures to be used in the treatment of this disease. They also desired particularly to determine whether it was feasible to accomplish retrograde decompression of the system of pancreatic ducts by resection of a portion of the tail of the pancreas and anastomosis of the gland to the small intestine or stomach. Specimens of pancreas obtained at autopsy in 16 cases of chronic pancreatitis encountered at the Mayo Clinic were studied with particular reference to the presence or absence of ductal dilatation. In 7 cases the duct of Wirsung was found to be grossly dilated in the tail of the pancreas. In 4 other cases, histologic evidence of dilatation was observed in the smaller ducts and ductules.

Factors probably contributing to the dilatation of the ducts were pancreatic lithiasis in 2 cases, choledocholithiasis in 2 cases, and foci of necrosis and inflammation in 3 cases. In the 4 cases in which histologic evidence of dilatation of small ducts and ductules was present, focal inflammatory foci or ductal metaplasia may have been responsible.

It is interesting that of all these mechanisms, only two, namely, choledocholithiasis and ductal metaplasia, can be related etiologically to pancreatitis. The other lesions that produce obstruction, such as pancreatic stones and necrotic and inflammatory foci, are generally thought to be the result of the pancreatitis. This does not, of course, imply that retrograde decompression of the pancreatic ductal system might not be effective in the treatment of chronic pancreatitis. Even though most of the obstructive lesions are not of etiologic significance, they may be important in the development of recurrent attacks and lead to progressive destruction of the gland if obstruction is not relieved. To this end, resection of the tail of the pancreas with anastomosis of the remaining portion of the pancreas to the jejunum or stomach is a method with potentialities for effective treatment. It is a much less formidable procedure than radical resection of the head of the pancreas, which eliminates the zone of obstruction of the pancreatic duct, or total pancreatectomy, which has been used in some instances of advanced disease.

Theoretic advantages of such retrograde decompression of the pancreas include reduction of the intraluminal pressure in the pancreatic ductal system caused by pancreatic secretions when the pancreatic duct is obstructed, and reduction of the effects of reflux of bile into the pancreatic ducts under pressure if such occurs. A practical consideration is the selection of cases of chronic pancreatitis in which retrograde decompression may be beneficial. Patency of the duct of Wirsung in the body and tail is essential. If dilatation of the duct in the tail and body of the pancreas is necessary for successful function after pancreaticojejunostomy or pancreaticogastrostomy, this procedure would be applicable only in selected cases of chronic pancreatitis. It is likely that dilatation of the pancreatic duct is not essential for the maintenance of such retrograde drainage, since clinical experience has shown that pancreatic fistulas are notoriously prone to stay open.

Carcinoma of the Head of the Pancreas; a Review of 49 Personal Cases. R. G. MOORE and J. D. YOUNGHUSBAND. *Brit. J. Surg.*, 1954, 41: 562.

THE authors review 49 consecutive cases of carcinoma of the head of the pancreas, common bile duct, ampulla of Vater, and duodenum, treated by them during the past 5 years.

In this series there were 21 males and 28 females. Four-fifths of the patients were over 60 years of age. Jaundice was the outstanding symptom. Twenty-two patients had pain. The incidence of itching was variable.

The most important physical finding was the presence of a palpable gallbladder (29 cases). Invariably the liver was enlarged. A separate mass was palpated in 5 cases. Stools were usually putty-colored, and the urine contained bile pigment.

In the pre-icteric phase, occult blood examinations, duodenal intubation, the secretin test, and radiology were most helpful. When jaundice was present, the most useful liver function tests were total and differential plasma proteins, the thymol turbidity test, gold and thymol flocculations, and alkaline phosphatase. Once the diagnosis of obstructive jaundice is made, operation should not be delayed.

Preoperative preparation included vitamin K, restoration of electrolyte balance, correction of anemia, high protein intake, breathing exercises, and postural drainage of the bronchial tree.

The advantages of a single operation are obvious; however, if the patient's condition necessitates a two-stage procedure, the authors recommend a simple external cholecystostomy as the first-stage plan. This leaves the surgeon free to employ any form of alimentary tract reconstruction that he desires at the second stage. The loss of bile is compensated for by oral administration of bile salts. No appreciable reduction in clinical jaundice can be expected before 2 weeks; the interval recommended between stages should be not less than 3 weeks.

The authors were able to make a confident diagnosis at operation in most cases by palpation alone. Biopsy is suggested only in doubtful cases, and if it fails to show carcinoma, a palliative operation should be done.

Tissue removed consisted of gastric antrum, pylorus, the entire duodenum with the first 4 to 6 inches of jejunum, enclosed pancreas, with as many related lymph glands as possible. The Whipple method of reconstruction was used, and, in addition, external cholecystostomy (with removal of the tube in 10 to 12 days).

Of the 29 patients considered suitable for radical operation, 18 survived and 11 died, an operative mortality of 38 per cent. Five patients who survived the operation died within 15 months of clinical carcinomatosis. Thirteen patients survived the operation and were free from signs of recurrence when last seen, the longest period of survival being 56 months.

The operability rate was 60 per cent. Inoperable cases had palliative operations aimed at relief of jaundice and occasional duodenal obstruction. Of these 18 patients, 5 failed to survive the operation, 8 survived for an average of 5 months, and 3 (recent cases) are still alive. —*S. Lloyd Teitelman, M.D.*

Results of Treatment of Carcinoma of the Pancreas. EDWARD S. STAFFORD, I. RIDGEWAY TRIMBLE, and JOHN N. CLASSEN. *Ann. Surg.*, 1954, 139: 800.

OF 37 PROVED cases of carcinoma of the head of the pancreas, only one patient is living 16 months after pancreaticoduodenectomy. The results are in accord with those reported by others. Despite the gloomy outlook, the authors believe it is fair to say that carcinoma of the pancreas must be attacked if it is to be cured. The gradual lowering of the operative mortality associated with pancreaticoduodenectomy ranks this operation at least as favorable a palliative procedure as the various biliary tract shunts.

It was seen that there is little difference in the period of survival from the time of onset of symptoms, whether a palliative procedure or resection is carried out. On the average, patients judged suitable for either type of procedure survived the onset of symptoms by only 12 to 14 months. This would suggest that the type of operative procedure had not influenced the course of the disease.

The difficulty of making an accurate diagnosis even at the operating table is admitted. In carcinoma of the pancreas, it is likely that only advanced unfavorable neoplasms will permit a successful biopsy to be taken from the head of the pancreas. If the biopsy shows no tumor, the duodenum is opened and a biopsy is taken from the ampullary area. If this, too, is unsuccessful, and if there are no evidences of distant metastases, resection is undertaken. It is realized that an occasional resection will be carried out for benign disease of the pancreas, but it is believed that this risk is justifiable in the attempt to cure patients who have cancer. Following removal of the head of the pancreas and duodenum, the authors prefer the one-stage Trimble method for re-establishing the continuity of the bowel. —*Stephen A. Zieman, M.D.*

MISCELLANEOUS

Factors Involving Wound Dehiscence; Study of 1,000 Cases. ROBERT L. MARSH, JOSEPH W. COXE, III, and G. ARNOLD STEVENS. *J. Am. M. Ass.*, 1954, 155: 1197.

FOR THIS study, wound dehiscence was defined as a wound separation including the peritoneum. The study included 1,000 laparotomies, exclusive of inguinal hernias and appendectomies through muscle-splitting incisions. Five-hundred of these laparotomies were performed at the Wadsworth Veterans Hospital in Los Angeles, and the author states that these cases were not as well controlled as were the second 500 cases which were done at St. John's Hospital and which were consecutive and completely controlled.

In the series of 1,000 patients operated upon at the Wadsworth Veterans Hospital, 322 had vertical incisions and 178 had transverse incisions. The average age of the patients was 50 years. Several types of wound closure were used. A layer closure was used in which the peritoneum and posterior sheath were closed with an absorbable suture of No. 00 or No. 0 chromic used as a running suture. In the anterior sheath and external rectus fascia, nonabsorbable sutures of silk or cotton, either No. 00 or No. 0, were used as an interrupted suture. The use of retention sutures was purely optional.

Of the patients with vertical incisions, 33⅓ per cent underwent emergency laparotomies, while only 17 per cent of patients with transverse incisions were emergencies. This incidence of emergencies was high as compared with the other series of cases, and it alone could account for the higher incidence of wound separation in these patients. Of the cases with vertical incisions, 44 per cent were classified as dirty cases, and of these the incidence of wound dehiscence was 10 per cent, whereas in the same group of cases with vertical incisions there was only a 5 per cent dehiscence in the 182 clean cases.

Of the 178 cases with transverse incision, 23 per cent were classified as dirty and in this group there was a 2 per cent incidence of dehiscence. A 2 per cent dehiscence rate also applied to the clean cases in the transverse incision group. The overall rate of dehiscence in the cases at the Veterans Hospital was 5.8 per cent.

At St. John's Hospital there were 500 well controlled cases and in all of these the type of wound closure was consistent. In the upper abdomen, through-and-through nonabsorbable retention sutures were used plus a layer closure of the peritoneum and posterior sheath with absorbable suture—a No. 00 chromic catgut used as a running suture. The anterior fascia was closed with a chromic No. 0 absorbable suture used as a running suture. In the lower abdomen, if carcinoma was present, the incision was closed exactly the same as that of the upper abdomen. In the case of an uncomplicated, clean, nonmalignant lesion, layer closure only was used, with No. 2 chromic catgut throughout.

Of the 500 incisions, there was a 1.6 per cent incidence of dehiscence, all of which occurred in vertical incisions, and none of which occurred in transverse incisions. The authors made a very definite effort, particularly in the closely controlled series of cases, to determine the factors responsible for the dehiscence. They felt definitely that the through-and-through retention sutures as used in the closely controlled series was the single most important feature in preventing dehiscence, but they did not feel that there was any evidence for or against transverse or vertical incisions, providing the latter were close to the midline and the trophic nerves were not interrupted. The important factors, in their opinion, predisposing to wound dehiscence were: (1) nutritional deficiencies incident to carcinoma, infection, or other debilitating factors; (2) mechanical factors, such as violent coughing and abdominal distention; (3) type of wound closure; and (4) age (the average age of patients with wound separation being 56 years as compared to an average age of less than 49 years for the 966 patients whose wounds healed primarily).

—Frederick C. Hoebel, M.D.

Mesenteric Chylangioma; with Report of 2 Cases. James G. Kanski. *Am. J. Surg.*, 1954, 87: 891.

Chylous cysts, sometimes called cholangiomas, are usually multilocular and occasionally occur as numerous small swellings of the mesentery, intestine, omentum, or retroperitoneal tissue. They are seen more commonly in the mesentery of the ileum and jejunum than in that of the colon; they may be simple or multiple, and may vary in size from that of an olive to an enormous growth.

Their etiology is obscure, and many theories have been offered to explain their formation. The contents of the cysts may be clear, milky, sebaceous, bloody, yellow, or brown. The cysts are benign, but malignant degeneration may occur.

The symptoms are not pathognomonic and a diagnosis is seldom made before operation. The presenting symptoms are most frequently those of an acute surgical complication, usually resembling intestinal obstruction. In uncomplicated cysts, a centrally located palpable tumor which is markedly mobile in the transverse direction may be found on examination. Pain may be generalized or localized. Roentgenologic examination is an aid in diagnosis because of increased or decreased density, opaque inclusions, or calcification within the cyst wall.

The most frequent complication of mesenteric cysts is intestinal obstruction. Other complications are hemorrhage into the cyst, torsion, or rupture of the cyst. The following operative procedures may be performed: (1) aspiration; (2) enucleation; (3) resection; and (4) marsupialization.

—Ely Elliott Lazarus, M.D.

GYNECOLOGY

UTERUS

Surgery in Connection with Double Uterus; Hemihysterectomy and Parietal Hysterosympexy (Chirurgie au niveau d'utérus doubles; hémi-hystérectomie et hystérosympexie pariétale). R. BOURG and G. LAMBERT. *Gyn. obst.*, Par., 1954, 53: 137.

SURGICAL CORRECTION of the double uterus may be done for a variety of reasons, but the most common indications are hematometra dysmenorrhea, ruptured pregnancy, hemorrhage, and adnexitis.

The operation usually performed is resection of one-half of the uterus at the level of the cervix. The tube and round ligament from the removed half can be transplanted into the remaining segment. Two cases illustrating this are described. One operation was performed because of pyometra and the other for a large leiomyoma.

In a few cases the segments of the uterus may be widely separated by a firm band of peritoneal tissue extending from the bladder to the cul-de-sac. Correction of this defect, as described for 1 case, consists of the rectangular excision of the medial surfaces of each uterine half. The margins are opposed with sutures and the peritoneal fold from the bladder is attached to the anterior uterine surface. This procedure is called parietal hysterosympexy.

—George C. Lewis, Jr., M.D.

Retention of Fragments of Fetal Bone in the Uterine Cervix for 10 Years (Rétention de fragments d'os foetal dans un col utérin pendant 10 ans). MARIANNE BASCH. *Bull. Féd. Soc. gyn. obst.*, 1954, 6: 10.

THE RETENTION of bony fragments within the cervical matrix is described in a case presenting a history of secondary sterility 10 years following an instrumental abortion of a 3 months' pregnancy. The patient had observed the passage of several small bony fragments. Here only symptoms were leukorrhea and subpubic pain. Hysterosalpingography and surgical excision of the endocervix revealed the presence of bone and cartilage. Their fetal origin was established by the presence of embryonic blood elements within the marrow.

In the discussion, 2 additional cases are mentioned. Both followed abortions at 3½ months. In one of these, menorrhagia and lower abdominal pain were the presenting symptoms; in the other, leukorrhea and metrorrhagia were noted.

—George C. Lewis, Jr., M.D.

Prophylaxis of Cervical Cancer; Its Diagnosis in Its Noninvasive State (Prophylaxie du cancer du col; son diagnostic à son stade non-invasif). P. FUNCK-BRENTANO. *Rev. fr. gyn. obst.*, 1954, 49: 1.

FOR YEARS the treatment of the lacerated infected cervix has been principally that of cautery with the more recent addition of antibiotics. However, the recent recognition of noninvasive cancer as a definite clinical problem has changed this approach to lesions of the cervix. The clinician now has available means for the detection of early premalignant changes, invasive malignancies, and the early noninvasive stage of cancer.

The steps that should be taken in the examination of the cervix should consist of a Schiller test, the vaginal smear, colposcopy, and the pathology examination of biopsy material. The Schiller test and colposcopy are invaluable in localizing the proper place to make the smear or take the biopsy specimen. The latter two procedures are complementary. Their advantages and disadvantages are discussed with reference to 12 cases of intraepithelial carcinoma discovered by the combined steps in detection.

Premalignant conditions and noninvasive carcinoma are defined and discussed with special emphasis on their arrest before invasive carcinoma can occur. The treatment of noninvasive carcinoma should be total hysterectomy with conservation of the adnexa.

—George C. Lewis, Jr., M.D.

Lymphoglandular Diffusion of Cancer of the Uterine Cervix (Sulla diffusione linfoghiandolare del cancro del collo uterino). PIETRO MARZIALE. *Clin. ostet. gin.*, 1954, 56: 1.

THE EXTIRPATED pelvic lymph glands were examined histologically in 66 patients with cervical cancer. These were women who underwent operation on the obstetrical and gynecological service of L. Cattaneo, at the University of Rome, in the period between January 1952 and July 1953. Sixty-one cases observed in this same Clinic in the period from 1946 to 1951 were reported by Russo (Atti Soc. ital ostet., 1951, 41: 379) with results which were not too different from the author's own.

Of the author's material, 48 patients underwent radical operation after the methods of Brunschwig and of Meigs. In the remaining 18 patients, the inoperability (in radical manner) of the condition present was recognized upon opening the abdomen. Here the same lymphadenectomy of the pelvic cavity was carried out together with ligation of the two hypogastric arteries and the two arteries of the round ligaments. The whole procedure was completed by bilateral extirpation of the adnexa. The purpose in doing this was to provoke a state of anemia, perhaps only temporary, of the tumor region, with the hope of its exercising an inhibitive influence upon the vitality and the development of the neoplastic cells during the subsequent period of irradiation therapy. The operation was always followed immediately by radium and subsequently by roentgen irradiation.

On the whole, lymphoglandular metastasis was revealed histologically in 20 per cent of the cancers in stage I; in 22.5 per cent of cancers in stage II; and in 52.4 per cent of cancers in stage III.

With reference to the incidence of involvement of the individual lymphoglandular groups, the author finds in his material that the order of decreasing incidence was as follows: the obturator glands, followed

by the common iliac and the external iliac. The hypogastric glands were involved twice in cases in the second stage, and 3 times in cases in the third stage; the sacral glands were involved once in cases in the second stage, and twice in cases in the third stage; the parametrial glands were involved once in second-stage conditions and the aortic glands were involved once in third-stage new growths.

From these figures, the high incidence of metastases to the pelvic lymph nodes in cancer of the uterine cervix is obvious, especially in patients with stage III tumors, and the importance of lymphadenectomy in these patients is understandable. These findings have so impressed the author's superior, Professor Cattaneo, that he has come to consider the problem of genital cancer—and consequently, also, cancer of the uterine cervix—as a glandular problem, and to regard radium and roentgen therapy of the infiltrated glands to be of limited efficacy.

The time is still too brief for evaluation of the effect of lymphadenectomy with regard to an improved prognosis for the patients; however, the excellent general condition in which the major number of patients are found leads to the hope of a lengthy period of survival. —*John W. Brennan, M.D.*

Pelvic Eviscerations in Cancer of the Uterine Cervix; Technique and Indications (Les pelvectomies dans le cancer du col utérin; technique et indications). COMTE and BOTTOU. *J. chir.*, Par., 1954, 70: 217.

FOURTEEN pelvic eviscerations during the past 2 years have been done by the authors at Casablanca, Morocco. Three of these were partial eviscerations (anterior pelvectomies) and the remaining 11 were total eviscerations.

The technique used was essentially that of Brunschwig and other American authors working in this field. Unlike these authors, the French surgeons construct, in the first session, a right-sided hypogastric artificial anus; later a left-sided double-barreled artificial anus is constructed and the right-sided anus is closed. The ureters are implanted in this lower colonic sac which later functions as a form of neovesical reservoir. Both the upper, or fecal, sac and the lower, or urinary, sac are evacuated by placing the patient in the left lateral decubitus position.

The operation is carried out in two stages—an abdominal session and a perineal session—and special effort is made at peritonization to bring down the greater omentum and suture it to the posterior peritoneum. Of course, the omentum must be long enough for this, and the desired result can not always be accomplished. Figures 1 and 2 in the original text show the different steps of the operation.

Two years is too short a period for the evaluation of ultimate results. However, the authors' experience, together with an evaluation of the results reported by other authors (Brunschwig, Meigs, Bricker, Parsons, and others) leads them to conclude that total evisceration of the pelvis is certainly justified in advanced conditions of cancer of the uterine cervix—principally recurrences following roentgen and radium irradiation and cases resistant to such treatment, in which the patient would otherwise be condemned to protracted suffering. In these instances the operation offers a chance of producing a fairly long survival with a tolerable existence, and as such the efforts of the surgeons in this field merit continuation.

For proper results, a well trained surgical team is imperative, as well as perfect conditions of anesthesia, equipment, and experience in the methods of re-animation and of blood transfusion. The operation will always necessitate a preoperative transfusion of 2 to 3 liters of blood. —*John W. Brennan, M.D.*

ADNEXAL AND PERIUTERINE CONDITIONS

Anatomoclinical and Histogenetic Considerations with Reference to the Tumor of Brenner; Apropos to a Personal Observation (Considerazioni anatomocliniche e istogenetiche sui tumori di Brenner; a proposito di un' osservazione personale). ENRICO FERRARIO. *Minerva gin.*, Tor., 1954, 6: 407.

THE AUTHOR'S PATIENT was a 65 year old woman who had given birth to a son. When 45 years of age she had undergone irradiation treatments for menorrhagia and metrorrhagia following the diagnosis of a submucous fibroid, and 5 years later she had undergone the same treatment for the same difficulty, however, this time there was noted an orange-sized tumor to the left of the uterus. The uterus itself was noticeably enlarged. Again the patient was apparently cured.

At the time of the last admission to the author's service, there were essentially the same symptoms, the uterus was again noticeably enlarged and there was a huge, football-sized tumor to the left of the uterus.

At laparotomy an oophorosalpingectomy was done, this including the tumor which had replaced the left ovary. The right ovary was small and sclerotic but appropriate to the age of the patient. The tubes were normal, and the uterus exhibited only a senile atrophic condition of the endometrium and a cherry-sized submucous fibroid. This fibroid explained the symptom of bleeding without the necessity for postulating an endocrine function of the tumor itself.

The tumor consisted of a solid basal mass and an upper cystic portion. The histologic findings were those of a typical Brenner's tumor. However, the tumor did not show any histologic evidence of invasion of the islands of epitheliallike cell nests by the stromal elements, such as is observed in the granulosa-celled tumors; therefore, these findings refute an origin from mesenchymal tissue. The environing stroma seemed to have been merely pushed aside and condensed as the result of expansive growth pressure.

There were present typical pseudomucinous cysts, lined by cuboidal epithelial cells which showed a tendency to become cylindrical in places, and nuclei displaced to the base of the cells, which were clear, without structured content, and very like in appearance to mucin-producing cells. However, at no point was there any clear evidence of metamorphosis from the Brenner type to the mucin-producing type. The tumor tissue was poorly vascular, but the lymph vessels within the cell nests were highly dilated, which was another suggestion of the pressure of expansive growth.

On the whole, from the study of his own patient and his review of the literature, it appears that the

author does not believe that the pseudomucinous cyst always develops from a Brenner tumor, nor does he believe that the Brenner tumor always develops from the so-called Walthard cell rests. He defines the Brenner tumor as a fibroepithelial neoplasm, usually benign and usually unilateral and confined in its location to the ovary itself. In the 1 instance in which the Brenner tumor was reported to be unrelated to the ovary in its origin doubt existed as to the authenticity of the diagnosis.

This does not mean, however, that the author believes that the Brenner tumor has an origin which is entirely different from that of the other neoplasms of the genital system of woman; in fact, he thinks that many of these neoplasms originate from the undifferentiated and therefore polyvalent tissues of the primordial mesodermic matrix of the genital ridge in the embryo. —*John W. Brennan, M.D.*

Removal of a 184 Pound Ovarian Tumor, and Observations Regarding Splanchnic Shock. Dan H. Eames, Jr., *Am. J. Obst. Gyn.*, 1954, 67: 1358.

The sudden release of acute intra-abdominal pressure has been said at times to cause the appearance of shock, commonly called splanchnic shock; this is most commonly reported to follow catheterization of a distended bladder, or the removal of large amounts of ascitic fluid or of large abdominal tumors. Unfortunately, there is little information in our literature concerning this phenomenon.

The ovarian tumor observed by the author was found to be the thirteenth largest reported, following an extensive review of the literature, and was the largest which had been removed intact. As such, with its comparatively sudden release of acute intra-abdominal pressure, it was believed to offer an exceptional opportunity for observations regarding the possible appearance of splanchnic shock.

Splanchnic shock due to a relatively rapid decrease in acute intra-abdominal pressure caused by removal of extremely large abdominal tumors is by no means constant in its appearance and is rather uncommon. When it does occur, it usually is manifested some hours following such a release in pressure, usually 4 to 24 hours later, and the use of "slow" decompression is poor prophylaxis. Instead, the most logical course of action seems to be the removal (intact) of such large tumors in order to face the possibilities of reaction with the patient in an optimum physical state.

With the use of whole blood and modern drugs this possibility has become secondary to the evils accompanying the drainage of any large ovarian tumor, and size alone should no longer be considered an indication for drainage rather than for intact removal.

—*John R. Wolff, M.D.*

Ovarian Carcinoma; Risk of Preserving the Ovary. Clyde L. Randall. *Obst. Gyn.*, 1954, 3: 491.

Approximately 70 per cent of ovarian neoplasms are discovered and removed before the patient's fiftieth year.

Physicians reporting malignancies to the Department of Health in upstate New York during the past 14 years have made it possible to calculate the probability that women will develop ovarian carcinoma. These data suggest that approximately 14 women per 1,000 will develop an ovarian neoplasm after 50 years of age, of which 8 will be malignant and 6 will be benign, and that the probability of the individual developing any malignancy decreases rapidly after her fiftieth year. The author questions the advisability of "prophylactically" removing grossly normal ovaries even after the menopause.—*Alan Rubin, M.D.*

MISCELLANEOUS

Tuberculosis of the Female Genitalia and Sterility; Considerations Based on a Series of 230 Treated Patients, of Whom 100 Were Operated Upon (Sobre tuberculosis genital femenina y esterilidad; consideraciones sobre 230 casos tratados, de ellos 100 operados). C. Fernandez-Ruiz. *Rev. espan. obst.*, Valencia, 1954, 13: 14.

It is not to be inferred that operation on these 100 patients was performed with genital tuberculosis as the indication; as a matter of fact, most of them were operated upon for other indications, including sterility, and the tuberculous involvement was uncovered by chance. Only rarely can tuberculosis of the tubes be diagnosed except by laparotomy. The only other diagnostic method which has been at all relied upon by the author's service has been that of hysterosalpingography. Even here, however, the author does not believe that the method is at all specific; the findings obtained (interrupted filling, sacciform dilatations, and general lack of homogeneity) can just as well be encountered in instances of nonspecific inflammatory processes. The author believes, with Schultze, that "tubal tuberculosis does not present characteristic roentgenologic appearances."

Surgery, however, in genital tuberculosis of the female is not limited to making chance diagnoses, but has a well delineated place in the treatment of this condition. The use of streptomycin and the other newer therapeutic measures does not fulfill the criteria of specific treatments. The antibiotics do not control the tuberculous lesions with poor circulatory supply. The province for these therapies is in the congestive processes and highly vascularized processes. Streptomycin and the niacin preparations will perhaps suppress acute disseminations and give protection against postsurgical spread of the tuberculous process, thus rendering surgery easier and more effective. On the other hand, surgery may render subsequent antibiotic therapy more effective; i.e., when the torpid fibrosclerotic lesions are removed, the ulcerating and congestive lesions rapidly come under control with the administration of antibiotics. In fact, in instances in which the specific and nonspecific inflammatory lesions are controlled by the antibiotics, the torpid avascular foci frequently continue to progress as before. Among the 100 patients who were operated upon, it was found necessary to perform radical procedures in 41 per cent. Of course, some of the radical measures were demanded by the presence of nontuberculous lesions.

With reference to the cure of infertility, the author's results have been very unsatisfactory. In the subjects in whom pregnancy occurred following treatment for

the genital tuberculosis, the treatment has always been strictly medical; that is, there has been no operative or biopsy confirmation of the clinical diagnosis of genital tuberculosis, and therefore the presence of specific involvement of the genitalia has not been definitely established. Such instances cannot, in the author's opinion, be cited in favor of any particular form of medical therapy.

Statements in the literature are cited with reference to the frequency with which pregnancies following cure of genital tuberculosis in the female eventuate in abortion, premature births, and tubal pregnancies, and the author concludes that although the possibility of the cure of infertility should always incline to a decidedly conservative attitude, the first aim of the physician should be the cure of the patient.

—*John W. Brennan, M.D.*

Pelvic Pain Based on a Vascular and Autonomic Nervous System Disorder. HOWARD C. TAYLOR, JR. *Am. J. Obst. Gyn.* 1954, 67: 1177.

A CLINICAL condition with characteristic symptoms and physical signs frequently encountered in gynecological practice is described. The principal complaints are various types of pelvic pain, with secondary symptoms dependent on excessive secretion from the cervix, minor changes in the character of menstruation, and bladder irritability.

The most likely explanation as to the nature of this disorder is that it is chiefly a disturbance of vascular physiology. For this reason the term "pelvic congestion" seems for the present a proper designation. Vascular change in the pelvic organs is produced physiologically by vasomotor impulses received over the pelvic sympathetic and parasympathetic systems. Pelvic congestion is then in a sense a "psychosomatic" disorder. Other factors, however, also affect the pelvic circulation, such as the steroid hormones, the anatomical supports of the uterus, and the position of the patient. Since these factors are also effective, pelvic congestion is not wholly "psychosomatic" in origin.

Therapy should be conservative with attention to the factors that may through nervous stress or emotional instability affect the pelvic autonomic nervous system. Logical treatment must also depend upon which factors affect the pelvic circulation locally, and should include care of the infected cervix and, if necessary, correction of relaxation of the pelvic floor or decensus.

In a few cases, when the pain is associated with enlarged ovaries and especially if the patient is sterile, conservative operations on the adnexa may be justified. In a few other cases in older women, if the disorder is of many years' standing and if other methods have failed, hysterectomy may be the therapy of choice.

—*Alan Rubin, M.D.*

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Clinicostatistical Study on the Incidence of Obstetrical Complications, with Particular Regard to Seasonal Influences During the 12 Year Period of 1941-1952 at the Obstetrical and Gynecological Clinic of the University of Padua, Italy (Studio clinico-statistico sulla frequenza della patologia ostetrica, con particolare riguardo all'incidenza stagionale, nel dodicennio 1941–52 nella Clinica Ostetrica e Ginecologica dell'Uñiversitá di Padova). G. FRANCO and A. ONNIS. *Arch. ostet. gin.*, 1953, 58: 459.

OF 14,454 DELIVERIES at the Obstetrical and Gynecological Clinic in Padua, Italy, during the period from 1941 through 1952, 2,514 (17.3%) were either preceded by complications of pregnancy, such as toxicosis, or were characterized by an anomalous presentation, by disease of the fetal adnexae, by uterine inertia, or by grave postpartum hemorrhage. Of the 2,514 complicated deliveries, 45.1 per cent comprised anomalous presentations, 21.7 per cent comprised toxicoses, 15.4 per cent exhibited uterine inertia, 14.1 per cent were instances of disease of the fetal adnexae, and 3.3 per cent were instances of postpartum hemorrhage. These figures coincide with those of some authors and differ from those of others. Where there is a divergence, the authors ascribe the discrepancies to differences in climate, race, and ambient factors; e.g., placenta previa occurs with greater frequency in women doing heavy work in the fields, and this occupation probably explains the incidence of this condition in the fall of the year—the season when this heavy labor is at its peak.

These seasonal variations of different pathological conditions are tabulated (in percentages) in the original text. The conditions listed are as follows: podalic presentation, shoulder presentation, face presentation, brow presentation, albuminuria, eclampsia, hyperemesis, uterine inertia, placenta previa, prolapse of the cord, polyhydramnios, vesicular mole, precipitate detachment of the placenta, and postpartum hemorrhage. Bearing this in mind, the results given in Table 22 of the original text should be obvious.

In the authors' opinion, a meteorological influence on this pathologic material, although not definitely demonstrated, may be presumed to be active in certain forms of uterine inertia which are not explained on the basis of other pathologic conditions causing postpartum hemorrhage and polyhydramnios.

—John W. Brennan, M.D.

Malignant Hypertension Supervening Rapidly on Pre-eclampsia. T. B. COUNIHAN and I. DONIACH. *J. Obst. Gyn. Brit. Empire*, 1954, 61: 449.

IT IS EXTREMELY RARE for pre-eclampsia to progress to a rapidly fatal malignant hypertension immediately following delivery; however, the authors report 2 such cases. Both women were normotensive in early pregnancy and afflicted by a flagrant pre-eclampsia in the last trimester with edema, albuminuria, and rapidly rising blood pressure. In spite of termination of the pregnancy, the toxemia merged into a state of progressive hypertension, retinopathy with papilledema, renal failure, and, finally, death from uremia in several months. In both, the illness was complicated by acute hemolytic anemia. Postmortem examination was carried out in each case.

The findings in the kidneys of both patients of occlusive fibroblastic intimal proliferation in the interlobular arteries, and of arteriolar and glomerular tuft fibrinoid necroses are thought to be diagnostic of malignant nephrosclerosis. Neither case showed lesions of an antecedent glomerulonephritis, pyelonephritis, or polyarteritis nodosa.

In 1 case treatment with methonium compounds failed to reduce the blood pressure. The coincident occurrence of acute hemolytic anemia is unexplained, but may have prognostic significance.

—Warren R. Lang, M.D.

Indications for, and the Scope of, Indirect Placentography in the Diagnosis of Placenta Previa. U. BORELL, I. FERNSTRÖM, and A. WESTMAN. *Acta obst. gyn. scand.*, 1954, 33: 231.

THE HOSPITAL RECORDS and roentgenograms of 192 pregnant women were reviewed. The patients had complained of painless vaginal bleeding during the last trimester of pregnancy and were examined by indirect placentography after the injection of a contrast medium into the bladder and of air into the rectum with mensuration of the distances between the presenting part and the bladder, rectum, and promontory. The normal measurements of these distances were defined.

It was found that this method is not reliable for diagnosis in the transverse and oblique views, in certain forms of breech presentation, and in some cases of head presentation examined earlier than in the last month of pregnancy. In such cases it is reasonable to use direct placentography, i.e., soft tissue roentgenography, or when this method is not applicable, arteriography should be used instead of indirect placentography.

—John R. Wolff, M.D.

An Instance of Intraepithelial Epithelioma of the Uterine Cervix Disclosed in the Course of Pregnancy; Electrocoagulation; Normal Epithelialization (Un cas d'épithélioma intra-épithélial du col découvert au cours d'une grossesse; electro-coagulation; epithélialisation normale). P. ISIDOR, R. CHASQUES, and J. FRADIN. *Bull. Fed. Soc. gyn. obst.*, 1954, 6: 40.

A 46 YEAR OLD multipara entered the clinic in the course of the eighth month of pregnancy, complaining of metrorrhagia. Examination disclosed a large ectropion of the cervix; implanted on the mucous surface of this ectropion was a cherry-sized polyplike growth. This mass was removed with the electric bistouri, after which the pregnancy proceeded to term, without further bleeding.

The polyp was covered by a stratified epithelium with faulty maturation, multiple and gigantic nuclei, and other evidences of cellular unrest, but no frank evidence of invasive malignancy.

Following birth of the child, a biopsy specimen was taken from the everted portion of the cervical mucosa. Since this surface looked pretty much the same, no special selectivity was exercised in choosing the place for the biopsy, and the findings were very much like those mentioned for the polyplike excrescence. Every 2 months these biopsies were repeated and the findings were always quite similar.

Finally, it was decided to remove the suspected area by means of an extensive and deep electrocoagulation, and to destroy in this manner the whole of the everted mucosa of the uterine cervix.

Since this procedure was carried out, more than a year has elapsed and repeated biopsies have consistently shown a normal mucosa and submucosa, without evidence anywhere of cancerous or precancerous changes.

It is the authors' hope that this single report may be of some aid in choosing between radical and conservative measures in the treatment of abnormal epithelial findings arising during pregnancy, and frequently tending to persist after childbirth. Certainly, such findings as those here described should not necessarily call for multilating surgery, especially in the young woman; an expectant attitude would seem to be justified in these instances. However, in the particular case cited, that of a 46 year old multipara, it is not intended that such an attitude should be generally adhered to; it is merely that in this older patient the expectant attitude was justified by the fact that the patient was unusually intelligent and cooperative. —*John W. Brennan, M.D.*

An Instance of Postabortive Perfringens Septicemia with Anuria, Treated by Exsanguinotransfusion and Typhomycine; Recovery (Un cas de septicémie à perfringens post-abortum avec anurie traité par exsanguino-transfusion et tifomycine; guérison). J. Lapeyrere and J. Ducos. *Bull. Fed. Soc. gyn. obst.*, 1954, 6: 120.

A THIRTY-THREE year old patient was sent in by her physician. She presented a peritoneal facies and evident signs of intense hemolysis. She was in complete anuria; the vaginal examination presented a soft, globular, painful uterus; the cervix was patent; the parametrium seemed little involved. The patient admitted attempts had been made to induce artificial abortion. A catheter and some gauze had been inserted 48 hours previously.

A clinical diagnosis of perfringens septicemia was made without waiting for the bacterial report, and treatment was started at once. An exsanguinotransfusion was started at once, and treatment with typhomycine (tifomycine) injected intramuscularly, was administered.

Diuresis was stimulated by daily injections of acetosterandryl. The fluids were watched and supplemented when indicated. Blood transfusions were later, though rarely, resorted to. Under this treatment the blood urea gradually diminished in amount and the general condition of the patient coincidentally improved.

Curettage was not done and hysterectomy was not considered, since it is common knowledge that typhomycine will suppress the perfringens. Under this drug the danger ceased to be microbial and became renal in character. Equally rejected were the splanchnic infiltrations and infiltrations of the renal pedicle. These measures do not appear to be more efficacious than the injections of novocain which were administered in this instance, or than the daily intramuscular injections of acetosterandryl.

Particularly stressed in this instance were the careful and continuous study of the volume of fluids, and the quantities of chlorides to be administered each day.

The authors believe that in this instance they have demonstrated the efficacy of typhomycine against perfringens septicemia, and they consider that this method should have a more general application.

—*John W. Brennan, M.D.*

Acute Tuberculous Hepatitis in a Pregnant Woman (L'hépatite aiguë tuberculeuse chez la femme enciente). Tevfik Remzi Kazancigil, Cezmi Kazancigil, and Mes'ut Vahdat. *Bull. Fed. Soc. gyn. obst.*, 1954, 6: 37.

IN THIS 25 year old primipara the vomiting and enlargement of the liver began following the third month of pregnancy. The liver extended downwards from the costal border for 5 fingerbreadths at the time of admission (end of pregnancy). A premature male infant was born. Puncture biopsy of the liver disclosed the presence of a miliary tuberculous hepatitis, shown in Fig. 1 in the original text.

As the temperature of the patient did not respond satisfactorily under heavy doses of penicillin, aureomycin, and streptomycin, recourse was had to nicotibine. On the fortieth day of treatment the fever disappeared and the patient left the clinic considerably improved; the uterus was involuted and the liver was smaller by 2 fingerbreadths. This was followed by a further course of nicotibine, and 1 month later the roentgenogram disclosed a spontaneous pneumothorax on the left side and an infiltration on the right. However, 3 months later the patient was found to have gained weight, the anemia had been largely corrected, and the liver had returned to its normal size. Total treatment consisted of 33,000,000 units of penicillin, 46 gm. of streptomycin, 300 mgm. of nicotibine 69 times, and 200 mgm. of nicotibine 13 times.

Two months after this last examination the patient returned to the clinic with an amenorrhea of two months' duration, nausea, and vomiting. There were symptoms of meningeal irritation. Curettage revealed tuberculosis of the endometrium, and roentgenologic examination showed bilateral pulmonary (miliary) tuberculosis. Nicotibine (250 mgm. per day) and streptomycin (1 gm. per day) were given; also, the first 5 days, streptomycin intraspinally (0.2 gm. daily). Under this treatment the temperature subsided and the cerebral symptoms disappeared.

Almost a year after this last attack the authors learned that the patient had died a few weeks previously of a generalized tuberculosis.

The authors' reason for publishing this single case history is that it presents so many aspects of the

problem of tuberculosis in pregnancy and shows how the antibiotics control the tuberculosis primarily, only to have it break out in other parts of the body, particularly during the year following termination of the pregnancy. —*John W. Brennan, M.D.*

NEWBORN

In Regard to 152 Births of Malformed Infants; Their Relative Frequency in Certain Periods of the Year (A propos de 152 naissances d'enfants malformés; leur relative fréquence à certaines époques de l'année. J. Ravina, J. J. Daunay, and P. Benamour. *Bull. Féd. Soc. gyn. obst.*, 1954, 6: 19.

During the period between October 1945 and December 1952, 152 births of malformed infants occurred at the Maternity of the Lariboisière Hospital, in France. In none of the cases was a specific etiologic factor discovered. The presumed dates of conception for all of the births were calculated and graphed with reference to their incidence and time period. The resulting curve showed that the greatest increase in the number of the conceptions occurred in the months between March and July in five of the years. There was no correlation with the date of conception for normal infants.

The authors state that the seasonal increase in malformation conceptions might be explained by the occurrence of infections, especially viral, during the first 3 months of gestation. The seasonal occurrence of specific defects is not discussed.

—*George C. Lewis, Jr., M.D.*

MISCELLANEOUS

High Oxygen and Hyaline-Like Membranes. Paul D. Bruns and Lloyd V. Shields. *Am. J. Obst. Gyn.*, 1954, 67: 1224.

Hyaline membranes can be produced in 75 per cent of guinea pigs by exposure to 98 per cent oxygen at sea level pressure from 40 to 100 hours. Experimental animals with oxygen-produced hyaline membranes that survive show no evidence of residual lung damage 5 weeks after exposure.

Specific and nonspecific staining reactions are similar in naturally occurring and experimentally produced hyaline membranes. This suggests a similar composition for all pulmonary hyaline membranes without inferring the same etiology for all types. From histologic comparison, pulmonary hyaline membranes in experimental animals and those in the newborn seem to be the result of injury to the alveolar duct and terminal bronchiolar structures.

Atelectasis and intracranial hemorrhage were frequently associated with hyaline membrane disease in infants but were not found in animals killed by exposure to high oxygen concentrations.

Aerosols of alevaire and alcohol behaved in a relatively nontoxic fashion and were accompanied by little hyaline membrane formation in experimental animals.

Animals given large doses of steroid hormones died rapidly in high oxygen with a fulminating type of pulmonary vascular injury. The possible significance of this finding is discussed.

Although high concentrations of oxygen (over 70 per cent at sea level pressure) given continuously and for prolonged periods to animals or human beings are injurious to pulmonary epithelium, certainly they are not the sole cause of hyaline membrane disease in the premature infant. However, high oxygen (over 70 per cent) can be an aggravating factor which may enhance pulmonary damage to the premature infant.

—*John R. Wolff, M.D.*

Adrenal Virilism in the Female Child and Adult. E. Stewart Taylor and Robert H. Snow. *Am. J. Obst. Gyn.*, 1954, 67: 1307.

Five cases of adrenal virilism are discussed. Two were instances of congenital adrenal hyperplasia resulting in pseudohermaphrodism, 1 was a case of acquired adrenal hyperplasia, and 2 were cases of virilism from adrenocortical tumors.

Adrenocortical hyperplasia causing virilism in the female may be successfully treated with cortisone. The anatomical abnormalities in the female produced in utero by adrenocortical hyperplasia usually can be corrected by rather simple surgical procedures. Urinary assays of the 17-ketosteroids and 11-oxysteroids are essential in order to classify properly the causes of virilism in the female child or adult.

—*John R. Wolff, M.D.*

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

Penetrating and Perforating Wounds of the Trunk with Renal Involvement; Observations on the Manner of Wounding, Character and Path of Missile, and Associated Injuries. FREDERICK A. LLOYD. *Q. Bull. Northwest. Univ. M. School*, 1954, 28: 308.

A MISSILE which perforates the body may produce renal injury if the kidney lies in its path. The missile may be from a pistol, a rifle, a machine gun, or from a high explosive shell. Wounds of the chest or abdomen are apt to cause multiple injuries and may include the kidney as well. Penetrating and perforating wounds in which the kidney is involved tend to follow a definite and recurring pattern, depending on the wound of entrance and the direction of the missile. Bullet wounds tend to be single. Wounds due to artillery shells and aeriel bombs, and land mines are frequently multiple.

In 16 patients, thoracoabdominal wounds were associated with renal involvement. In only 7 cases was the kidney alone injured by a bullet. The article contains many diagrams showing wounds of entry and exit, according to which injury to the kidney may be predicted. —*S. Richard Muellner, M.D.*

Puncture Biopsy of the Kidney (La ponction-biopsie du rein). F. REUBI. *Helvet. chir. acta*, 1954, 21: 128.

IN ILLUSTRATING the possible dangers of this method of examination, the author cites the occurrence of a large hemorrhage following puncture of the kidney parenchyma which apparently so interfered with the only functioning kidney in its pyeloureteral drainage system as to induce a fatal anuria. Other dangers are: infection (do not puncture in the presence of abscess), perforation (of thin parenchyma in huge hydronephrosis), and insufficient renal reserve (reflex anuria); however, when these possibilities are kept in mind (prophylactic hemostyptics) he believes that the method is fairly innocuous.

Some of the advantages to be derived from the method are cited.

In one instance the diagnosis of a subacute and chronic glomerulonephritis without increased arterial tension, retinal signs, and with normal nonprotein nitrogen was confirmed by puncture biopsy. The biopsy presented a typical histologic appearance of an intracapillary, membranous glomerulonephritis (or glomerulonephrosis).

In the second instance there were acute symptoms of a glomerulonephritis which cleared up, except for a residual albuminuria. The puncture biopsy on the 176th day of hospitalization disclosed minor lesions in some of the loops. The meager extension of the lesions demonstrated how the renal function could apparently return to normal, but leave a persistent albuminuria.

In the third instance, during numerous hospitalizations for recurring pyuria with temperature elevations and pain in the region of the kidney (particularly the right kidney), the diagnosis wavered between a glomerulonephritis and a chronic pyelonephritis. Here the biopsy specimen disclosed the lesions of chronic glomerulonephritis with endothelial and epithelial proliferation of the loops and the capsule of Bowman.

In conclusion, the author is hopeful that with the proper consideration of indications and the proper degree of discretion, it will be possible to render the technique as harmless as ureteral catheterism and ascending pyelography. —*John W. Brenann, M.D.*

New Procedures for the Functional Exploration of the Kidney (Nouveaux procédés d'exploration fonctionelle des reins). J. TRAEGER. *Helvet. chir. acta*, 1954, 21: 137.

TWO HUNDRED clearance tests have been done on the author's service (Urologic Clinic of J. Cibert, Lyon, France) and the results are compared with those obtained with inulin. These results have proved entirely comparable. The author's work has been done with sodium hyposulfite for determining the state of glomerular filtration. Tests with para-amino-hippuric acid (PAH) were run simultaneously in order to help gain an idea of the functional capacity of the renal tubules, particularly with the purpose of gaining some conception as to whether any discrepancies were the result of malfunctioning of the tubules themselves or the result of variations in the blood supply to the kidney.

The technique and the modus operandi of these test substances are fully discussed in English by Homer Smith (The Kidney. *Oxford Medical Publications*, New York: 1951), and in French by Hamburger and Ryckewaert (Nouveaux procédés d'exploration fonctionnelle du rein. Flammarion: 1949). Of course, these writers have considered the subject purely from the standpoint of research, while the present author considers the subject from the practical standpoint.

Although less is known about the value of these tests when applied to the pathologic kidney or the kidney functioning in the presence of cardiovascular conditions (hypertension, etc.), nevertheless the author agrees with Reubi (*J. appl. Physiol.*, 1950, 3: 63) that the errors inherent in the method with sodium hyposulphite are not of such moment as to condemn the method for practical application.

In view of the rather important and inexplicable variations in plasma content of the hyposulphite and of the PAH with a single intravenous injection, the author prefers continuing the initial injection of these substances by a perfusion containing small amounts of these drugs. In this manner the plasma content is kept more stable. Two clearance periods are carried out and the average of the results taken as the most accurate obtainable. The author procures the urine for the urinary titer by means of catheterization of the bladder; he does not think individual catheterization of the ureters is necessary, since the pathological kidney is practically always nonfunctioning.

The practical indications, for purposes of diagnosis, therapy or prognosis, are much more limited than are those for purposes of research especially since, with the advent of nitrogen retention, the tests are no longer of much value; yet these tests do represent an excellent means of investigating the renal function—one that cannot be replaced or substituted for. These tests are chiefly of value in those conditions which are included in the renal affections extending from the beginning of the renal involvement up to the appearance of nitrogen retention.

With the above restrictions in mind, the author believes that the tests are of value for determining the degree of renal insufficiency in the course of a tuberculosis, an ascending nephritis, a polycystic kidney, etc., particularly when one is sure that the lesion is in a chronic stage. The knowledge gained by this method of investigation is of particular interest in the field of the hypertensive diseases. Here it is particularly advantageous to know whether the hypertension is of the essential type or is secondary to a glomerulonephritis. Of course, this work does not come strictly within the domain of the urologist. The urologist becomes interested in those instances of hypertension which are secondary to a unilateral renal lesion. In these instances the problem is to know if the lesions of the apparently healthy kidney are of such a character that they will regress under treatment. If the diminution of the glomerular filtration results from a glomerular sclerosis, it is practically certain that the lesion will not regress and that the final course of the condition will move towards the condition of renal insufficiency. On the contrary, if the glomerular filtration is not affected, if there are indicated only changes in the blood supplied to the organ, one may expect that the hypertension will be reversible, at least if the lesions of the adelphic kidney are transient ones.

The author concludes with the thought that, although the repugnance which the practicing physician feels towards those who utilize the methods promulgated, on their patients, for mere purposes of pure research, yet it would be unjustifiable to neglect them in those instances where they are able to provide the indications for purposes of diagnosis, therapy and prognosis. —*John W. Brennan, M.D.*

The Classical and the Modern Tests of Renal Function in Urologic Practice and Research (Klassische und moderne Nierenfunktionspruefungen in der urologischen Praxis und Forschung). J. MINDER. *Helvet. chir. acta*, 1954, 21: 155.

THE RENAL function tests are discussed from the standpoint of a practicing urologist. It is considered that the most important methods of evaluation of kidney function are those of urography and chromocystography. These two techniques will suffice in approximately 90 per cent of instances; however, the concentration and dilution tests and the determination of the nonprotein nitrogen retain their previous significance.

The significance of the determination of the clearances as a means of evaluating the functional capacities of the individual kidney, in combination with catheterization of the ureters, has not proved of value in urologic practice; for the evaluation of the total capacities it is primarily of theoretical value; practically it can be dispensed with in most instances, since it is needed in only a few conditions. A great deal of this reluctance on the part of the urologist to use the clearance test extensively lies in the difficulties involved in the technique and personnel and, particularly in the amount of time demanded; therefore, a method of accomplishing the same end more simply would be welcomed. It is for this reason that the author speaks favorably of the possibilities inherent in the half value-time determinations proposed by HARD, since this method (consisting simply of injecting phenol red and determining the length of time for the resulting plasma value of this substance to sink to half its original titre) is simple of application and is independent of any diuretic effect. This attitude is objected to by REUBI in his discussion of the lecture. REUBI asserted that when the clearances are to be determined, the technique must be of the most rigorous and precise nature, and it is for this reason that he objects to the half value-time determinations of HARD. However, MINDER replies that he merely suggested that in instances of urinary retention it would be ideal to gain an exact knowledge with reference to the clearance values, and that they should be determined just as are the values of nonprotein nitrogen and the other functional tests, and for this reason he would welcome any possibility of simplifying the method and shortening the determination time.

In conclusion the author states that none of the functional tests tells everything, and none can be properly understood without considering the disease picture as a whole. Every functional test must be regarded as a partial manifestation of the entire nosologic entity and it is the chief duty of the urologist to fit the individual functional test into the entire picture of the clinical and physiological behavior of the patient. The chronically diseased kidney—the nonkidney of the physiologist—is encountered daily by the urologist and his only question is: how long, and to what extent (considering the great capacities for adaptation and variability in the function of the organ), is the diseased kidney still a kidney? Where are the limits of its reparability to be found? Here, in the author's opinion, is the most important as well as the most interesting field of endeavor for the urologist.

—*John W. Brennan, M.D.*

Neoplasms of the Ureter. J. H. J. VAN DER VUURST DE VRIES. *Arch. chir. Neerl.*, 1954, 6: 82.

Two hundred and four cases of ureteral tumors had been published prior to the 4 cases herein presented. Of the 4 herein presented, 1 was a papilloma, the second was papillomatosis with a metastatic bladder lesion (carcinoma), the third was papillary carcinoma of the kidney, ureter, and bladder, and the fourth case was papillomatosis of the ureteral stump.

A triad of symptoms seen in ureteral tumors is similar to that in renal tumors: (a) hematuria, (b) pain due to obstruction, and (c) tumor mass due to hydronephrosis following obstruction.

The author adds some cases to the literature, but adds nothing to the diagnosis or therapy of ureteral tumor. —*John R. Herman, M.D.*

A Contribution to the Clinical Picture of Ureteral Tumors with Particular Reference to the Benign Primary Tumors (Ein Beitrag zur Klinik der Harnleitergeschwuelste unter besonderer Beruecksichtigung der gutartigen primaeren Tumoren). T. BURCKHART, E. SCHMIDT, and W. BUSANNY-CASPARI. *Zschr. Urol.*, 1954, 47: 214.

THE PATIENT was a 33-year-old housewife who had been suffering for about a year from pains of changing location and intensity. These pains were always located in the region of the right flank, at times radiating downwards to the bladder. They developed about four times monthly, but recently were becoming more frequent and more severe. In the pain-free intervals there persisted of late a dull sense of pressure in the region of the right flank. There had been no loss of weight. After the attacks of pain, traces of albumin were repeatedly observed in the urine.

Intravenous pyelography disclosed on the right side some increase in size of the upper urinary passages, including the upper third of the ureter. At the level of the upper edge of the third lumbar vertebra the shadow of the ureter ended suddenly on a broad base. Further down, the course of the ureter was represented by a threadlike tracing of contrast material.

On cystoscopy the ureteral apertures appeared to be normal on both sides; the spurts of urine on the right side appeared to be less vigorous than on the left, and the appearance of the day's urine on the right side was somewhat delayed.

Introduction of the ureteral catheter was easily accomplished on both sides, and on neither side was bleeding induced by the procedure. Retrograde pyelography disclosed on the right side a markedly dilated urinary passage cavitary system with spindle-shaped enlargement from the third to the fifth lumbar vertebral levels of the ureter. This stretch of ureter exhibited deposits of contrast material, peripherally outlining the ureteral lumen.

At operation the dilated portion of the ureter was opened and a 10 cm. long, finger-thick tumor was removed. The growth was attached to the ureteral wall above by a slender pedicle. This pedicle was cut through and its base cauterized.

Histologic examination of the excised tumor disclosed the presence of a benign neoplasm having the nature of a soft fibroma. The stroma was very coarsely textured and the interstices were filled with a collagenous material; that is, an acidic mucopolysaccharidic substance. The tumor itself was rather irregularly lobed, but its individual lobules were smooth-surfaced and covered with a low cubical epithelium which presented more than one layer only in some of the deep indentations.

On control examination, 10 months later, there was no longer pain and no evidence of blood in the urine. On the intravenous pyelogram the cavitary system of the right kidney and renal pelvis was still dilated and the right ureter displayed evidence of dystonia.

Two photomicrographic reproductions illustrate the histological characteristics of the tumor.

The authors believe that the rarity of primary benign tumors of the ureter and the interesting aspects of the present case justify its publication here.

—John W. Brennan, M.D.

BLADDER, URETHRA, AND PENIS

Radical Cystectomy for Advanced Carcinoma of the Bladder. EMILE SAYEGH. *J. Urol.*, Balt., 1954, 71: 715.

THIS IS a report comparing the results of bilateral transplantation of the ureters, bilateral ureteral transplantation with total cystectomy, and bilateral ureteral transplantation with total cystectomy and pelvic adenectomy in the treatment of advanced carcinoma of the bladder. A total of 106 patients with bladder tumors deeply infiltrating the muscularis, serosa, and perivesical space and with enlarged lymph nodes was treated. Twenty-one patients were treated by ureteral transplantation alone. None of these survived the second year. Twenty-three patients were treated by ureteral transplantation and total cystectomy. None of these survived the third year. Sixty-two patients were treated by a combination of total cystectomy, pelvic adenectomy, and bilateral ureteral transplantation. Eight patients in this group are alive after 3 years and 3 are alive after 4 to 6 years. Eleven patients are alive 1 to 2 years after this procedure; 2 have lived 2 to 3 years. There was little difference in the immediate mortality from the various types of procedures.

From this study the author concludes that in the treatment of advanced carcinoma of the bladder, bilateral transplantation of the ureters alone or in combination with total cystectomy is unsatisfactory. The best palliative results were obtained when bilateral ureteral transplantation was combined with total cystectomy and pelvic node dissection. In some instances the procedure apparently resulted in the complete extirpation of the growth.

The author points out certain precautions which may lead to better results from radical cystectomy for extensive bladder tumors. Among these are the high section of the ureter because of the likelihood of involvement of its muscular coat by tumor, the removal of an appreciable segment of the urethra in treatment of tumors involving the base of the bladder, and the ligation of all vascular connections to the bladder prior to extensive manipulation. Evidence is presented which emphasizes the importance of avoiding spillage of tumor during the operative procedure.

—John T. Grayhack, M.D.

Reconstruction of the Anterior Urethra in Hypospadias by the Buried Skin Strip Method; a Simplified and Improved Technique. J. C. MUSTARDÉ *Brit. J. Plast. Surg.*, 1954, 7: 166.

THE AUTHOR reports 12 cases of hypospadias repair in which a successful fistula-free reconstruction of the anterior urethra was obtained in 11 cases. In the content of the article, however, it becomes apparent that at least 3 patients developed some necrosis and a fistula. One failure was due to catheter pressure, 1 to pressure of the clamp, and 1 to hemorrhage.

The method of repair was based on the Duplay method. A small strip of skin is circumscribed on the surface of the penis, extending around the urethral orifice and down to the under surface of the glans. This is from 5 to 7 mm. in width. Lateral flaps of penile skin are elevated and then closed over the skin strip. A small catheter was laid along the skin strip into the urethral orifice and the lateral flaps were closed over the catheter

in some cases. In other cases a perineal urethrostomy was performed and drainage was effected through the opening.

The editor has devised a plastic acrylic cylinder which fits over the penis slit along one side and the blades or flanges formed along the slit. There is a screw clamp arrangement and tightening of the screw apposes the two flanges. The two lateral flaps of penile skin, when sutured together, are drawn down between the flanges. As the flanges are tightened the skin flaps are apposed "back to back" along the length of the reconstruction. The plastic clamp is supported in an erect position by an abdominal pad and taped in place for 7 to 10 days. When it is removed, the skin edges have healed together beneath the flanges.

—*C. Barber Mueller, M.D.*

GENITAL ORGANS

Experience with "ST 52-ASTA" in the Treatment of Prostatic Cancer (Erfahrungen mit "ST 52-ASTA" bei der Behandlung des Prostatakarzinoms). R. Carow. *Zschr. Urol.*, 1954, 47: 81.

Estrogenic hormone therapy of prostatic cancer is believed to influence the production of androgenic substances and have an indirect effect on the function of the anterior pituitary lobe. According to Druckrey and Raabe, diethylstilbesterol has a cytostatic effect in addition to its estrogenic influence. In the treatment of prostatic cancer a maximum cytostatic effect on the prostatic cancer cell is desirable. An ester of an estrogen made with phosphoric acid becomes water soluble and is thus converted into an ineffective form (transport form). However, when this ester reaches the prostatic cancer cell the acid phosphatase of the cancer cell sets free the cytostatic portion of this substance, which then becomes locally deposited and therefore has its maximum effect at the local level (Druckrey and Raabe). Since the activity of the acid phosphatase is much greater compared with that of the alkaline phosphatase, a selective splitting of the stilbesterol phosphate ester in the prostatic cancer cell occurs. The amount of alkaline and acid phosphatase in the blood and in other tissues is so small that it has very little effect on the stilbesterol phosphate. The intact phosphate, therefore, remains inactivated in the blood stream. By utilizing the acid phosphatase in the prostatic cancer cell, a greater cytostatic effect on such cells can be achieved and side reactions from large doses of this drug can thus be avoided.

In the laboratories of the Asta Company, Arnold synthesized diethyldioxystilbesteroldiphosphate as the diosodium salt, according to the suggestion of Druckrey and Raabe. The salt was called St 52-ASTA. One 5 c.c. ampule contained 250 mgm. of this substance for intravenous injection. Ten carefully selected patients were treated with this drug. These patients received a daily injection of 250 mgm. of St 52-ASTA. In some cases 500 to 2,000 mgm. were given without side reactions. Gynecomastia did not occur.

In general, the patient showed a very rapid objective and subjective improvement. In most instances, residual urine disappeared in a very short time with this therapy, without the need of transurethral resection of the prostate. The decrease in the hardness of the gland and the shrinkage of the nodules appear to occur more quickly with St 52-ASTA. The roentgenographic appearance of bone metastases did not seem to be influenced by it. Patients who failed to make any sort of progress with previous hormonal therapy or those whose gland failed to recede any further, and who persistently carried elevated acid phosphatase levels, showed benefit from the new medication. In each such case, the acid phosphatase level was brought down to normal limits within a short time. The author believes quite strongly that the intravenous use of the phosphorylated diethylstilbesterol St 52-ASTA is more effective than estrogenic hormones used either by the oral route or by implantation.

—*S. Richard Muellner, M.D.*

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Observations on the Course of Skeletal Tuberculosis Under the Influence of Antibiotics (Beobachtungen ueber den Verlauf der Skelett-Tuberkulose unter der Einwirkung der Tuberkulostatika). K. DAUBENSPECK and E. RAUSCH. *Zschr. Orthop.*, 1954, 85: 5.

ANIMAL EXPERIMENTS revealed that antibiotics are able to protect organs not yet infected, in most instances, and to prevent tuberculous infection in the human body. Resistance to certain antibiotics demonstrated in laboratory experiments does not necessarily indicate resistance to the antibiotic in humans. The advantages of the administration of various antibiotics and their side effects are discussed. Particular attention is given to streptomycin and INH and to thiosemicarbazon and PAS. Paratebin and oxyprocainpenicillin are also discussed.

In 47 per cent of all cases of tuberculous spondylitis an abscess was found. The authors differentiate between the abscess formation in an acute process and that in a chronic process. In the acute phase the abscess is continuously filled with fresh infectious material; in the chronic phase there is only a collection of tuberculous pus and detritus. The early diagnosis of tuberculous spondylitis is difficult. There is usually an increase of "night pain." Initially, splintering of the spine and a decrease of the intervertebral space is often seen on x-ray examination. As a rule, the treatment is conservative with immobilization in plaster and heliotherapy with antibiotics. Operative treatment consists of excision of the tuberculous foci and possible fusion of the spine according to the Henle-Albee method. With conservative therapy, the disease is prolonged for 3 to 6 years. Active pulmonary tuberculosis apparently is not a contraindication to spinal fusion. Immobilization in plaster apparently is beneficial, even to the pulmonary process. The presence of an abscess within the operative field is considered a contraindication to surgery. The appearance of an unexpected caseous focus within the field of operation is not a contraindication to spinal fusion; the focus is excised and the bone graft is placed along the spinous processes. The author places paratebin into the wound. Operations are usually well tolerated and the condition is improved. —*George I. Reiss, M.D.*

Tuberculous Cystic Osteitis (Osteiti cistiche di natura T.B.C.). L. PELLEGRINI. *Arch. Putti chir. org. movim.*, 1953, 3: 271.

SKELETAL TUBERCULOSIS may appear in lacunar cystic form. Its signs are: circumscribed foci of rarefaction, well outlined, ovoid, or round which are situated juxta-articularly in the long bones, but rarely in the flat ones (pelvis). A sclerotic ring may surround the foci but only in the older lesions. This consists of irregular accumulations of calcium, not of thickening of the trabeculation. Twenty years ago Jungling described this lesion as "tuberculosis cystica multiplex."

The author describes 4 typical cases with localization in the femur, the os ilii, and the humerus. In all of the patients a tuberculous condition (pleuritic or glandular) preceded the bone involvement, which facilitated the diagnosis. All of the patients also developed cold abscesses eventually. The clinical course was marked by moderate pain (often with nocturnal exacerbations), slight fever, and functional impairment. In the early period when the roentgenogram was still negative the diagnosis was based on the previous tuberculosis history, the temperature, and the ineffectiveness of penicillin given in large doses.

Differentially, one must consider solitary cysts, giant cell tumors, osteosarcomas, chondromas, myelomas, connective tissue tumors, lues, and osteomyelitis. The cases again demonstrate the polymorphism of tuberculous manifestations of the skeletal system. —*Arthur Steindler, M.D.*

The Chemotherapy of Orthopedic Tuberculosis. F. HARWOOD STEVENSON. *J. Bone Surg.*, 1954, 36-B: 5.

THIS PRIZE-WINNING ESSAY deals with the results of the treatment of tuberculosis of the bones and joints with para-aminosalicylic acid, streptomycin, and isonicotinic acid hydrazide. Para-aminosalicylic acid was introduced in 1946 by Lehmann, and has only limited usefulness when used alone in pulmonary or orthopedic tuberculosis. Its most useful effect is the prevention of the emergence of streptomycin-resistant strains of the tubercle bacillus when it is used in conjunction with streptomycin. A dose of 10 to 20 gm. a day is necessary for this action, and reactions of toxicity, which fortunately are usually mild, are fairly common.

Streptomycin sulfate is less painful when injected intramuscularly than is the calcium salt, but is as effective as the latter. A single daily dose was found to be as effective as divided doses. Although 2 gm. daily is a more effective dose than the smaller one, the great toxicity of such a quantity makes this dose prohibitive for continued use, and a 1 gm. dose daily is the accepted routine. This quantity of streptomycin is usually combined with 12 gm. of PAS and given daily, but recently the same dose administered twice weekly has been found to be as effective as when given daily. The most important toxic effects of the streptomycin are associated with the eighth nerve. The deafness is permanent, but the vertigo can be compensated, except when the patient is in the dark. Symptoms of deficiency of vitamin B also develop, but can be easily controlled with high doses of the vitamin.

Isonicotinic acid hydrazide, commonly referred to as INAH has been used in doses of 3 to 8 mgm. per kilogram of body weight. Because of its ability to penetrate the cells and affect the tubercle bacilli within them, it has a synergistic effect when combined with streptomycin.

In summary, the author recommends 1 gm. of streptomycin daily, 4 mgm. of INAH per kilogram of body weight and 15 gm. of PAS daily as the accepted chemotherapy of orthopedic tuberculosis.

In the remainder of the article the author analyzes comparable series of cases of tuberculosis of the bones and joints to determine the effectiveness of chemotherapy as outlined. From these studies he concludes that streptomycin produced a better range of motion at the end of treatment in 40 per cent of the treated patients, and that the length of conservative treatment was reduced by 50 per cent. These differences were less distinct in cases of extra-articular tuberculosis. Also, it was found that synovial tuberculosis in young adult persons is best treated with streptomycin administered intramuscularly and intra-articularly, and with rest in bed without splinting of the joint.

The author's suggestions as to treatment are:

1. For synovial disease of the knee
   a. In children: 3 months' use of streptomycin and an average duration of splinting of 7 months
   b. In young adults: intra-articular and intramuscular use of streptomycin, PAS, and INAH, without splinting but with rest in bed
2. For intra-articular foci of the hip: streptomycin, PAS, and INAH.
3. For tuberculous abscesses: drainage of abscess under cover of streptomycin and eventual secondary closure
4. For tuberculous sinuses: streptomycin must be used in conjunction with surgical attack on the underlying disease.

—*E. W. Johnson, Jr., M.D.*

Chemotherapy of Tuberculosis of the Bones and Joints. M. C. WILKINSON. *J. Bone Surg.*, 1954, 36-B: 23.

THE PRINCIPAL ANTIBIOTIC AGENT studied in this essay was streptomycin. Since there is evidence to substantiate the view that resistant strains of the tubercle bacillus do not develop in extrapulmonary tuberculosis, little para-aminosalicylic acid was used in this study.

The conditions of groups of patients were compared to determine the efficiency of constitutional treatment as against antibiotic treatment only. These groups were further broken down as to the location of the bone involvement. The conclusions drawn were that streptomycin reduces the length of treatment necessary, but is not of itself a major curative agent. There is no evidence to show that it can supplant constitutional treatment.

Also, an attempt was made by the author to determine the effectiveness of streptomycin as an adjunct to definitive surgical intervention in tuberculous lesions. A total of 97 patients were operated upon, some of whom had received streptomycin 20 days, and some more than 90 days, preoperatively. The conclusions from this part of the study were: (1) the effect of streptomycin on tuberculous tissue was more marked after 90 days of administration, (2) the effect of streptomycin on tuberculous bone and granulomas was slight, and (3) the effect of streptomycin on synovial tissue was more marked. To summarize, the author thought that in established osseous lesions the amount of improvement attributable to streptomycin was not marked.

As a final conclusion, the author states that antibiotic therapy may well be curative in early tuberculous disease, since in the early stage access to the organism is ready. However, as necrosis and ischemia develop in the latter stages, chemotherapy must be used as an adjunct to other forms of therapy, constitutional and surgical.

—*E. W. Johnson, Jr., M.D.*

The Natural History of Osteoid Osteoma; with a Report of 20 Cases. J. S. R. GOLDING. *J. Bone Surg.*, 1954, 36-B: 218.

THE AUTHOR presents 20 cases of this relatively new and interesting clinical entity, osteoid osteoma. Males are affected more commonly than females; the onset of symptoms usually is in the second decade, and severe but poorly localized pain is the cardinal complaint. There is no relationship of the disease to trauma. Atrophy and limp may be present, as may be local heat and tenderness. Results of the customary laboratory procedures are within normal limits. Roentgenologically, the lesion produces a zone of bony sclerosis surrounding an area of radiolucency which is never more than 1 cm. in diameter.

Grossly, the lesion appears as a vascular mass of a red to light orange color. The diameter ranges from 3 to 10 mm. Microscopic examination discloses a well circumscribed mass of irregular osteoid tissue which lies in a highly vascular stroma of connective tissue, the whole being surrounded by thickened trabeculae of highly vascular bone.

The literature contains considerable indirect evidence that osteoid osteoma runs a self-limited course. The condition of one of the author's patients—for whom biopsy unfortunately was not done—was followed up for 6 years, and almost complete cessation of the symptoms was noted. This concept of the natural termination of the symptoms is developed by the author. To expand this theme he likens osteoid osteomas to benign angiomas, some of which regress spontaneously. This regression is thought to be due to thrombosis of the vessels within the angioma, and this cause of regression is thought to be present in osteoid osteoma also. However, the author does not produce proof for this hypothesis.

It is generally accepted that complete excision is the treatment of choice.

—*E. W. Johnson, Jr., M.D.*

A Peculiar Joint Disease: Systemic Calcification of Articular Cartilage (Sopra una particolare malattia articolare: l'incrostazione calcarea sistemica delle cartilagini articolare). R. MARZIANI. *Arch. Putti chir. org. movim.*, 1953, 3: 220.

THE AUTHOR has been unable to find any reference to systemic calcification of articular cartilage in the literature. His case was that of a man of 28 years who was seen in February, 1952. The first symptoms appeared in 1945, consisting of pain and swelling of the knees, shoulders, and wrists which disappeared shortly on antirheumatic treatment. Three years later a similar attack occurred and after 3 more years a third one occurred.

In the third attack there was articular grating in the left shoulder; distention with muscular atrophy of the left knee; and slight grating in the right knee. Roentgenograms revealed that the cartilaginous contours and the menisci were lined with a slender radiopaque zone which did not extend to the synovia. A similar shadow was seen in the right knee, the acromio-

clavicular articulation, and the shoulders, elbows, and wrists. Laboratory examination showed alkaline phosphatase 20 mgm./per cent; calcium in the synovial fluid 24 mgm./per cent; while the plasma was normal (11 mgm./per cent).

The disease involved many articulations, was systemic in character, and was marked roentgenologically by calcium incrustations of the cartilage and fibrocartilage. Clinically, there were signs of articular pain which yielded to antirheumatic remedies. One point of interest was the high synovial content of calcium. Inasmuch as the plasma calcium was normal, the condition could not have been caused by hypercalcemia. The calcium incrustation came from the precipitation of the synovial calcium; the passage of calcium from the incrustation back to the liquid occurred in relation to the phases of the disease. The disease is one of long duration (years), with remissions peculiar to polyarthritis rheumatica without fever.

—Arthur Steindler, M.D.

Hydrocortisone in Tennis Elbow. D. E. Freeland and M. de G. Gribble. *Lancet.*, Lond., 1954, 2: 225.

The authors present 2 small series of cases of tennis elbow. In one series, treatment consisted of hydrocortisone injection; in the other series, local procaine injection. In both series, injection was at the site of maximum tenderness over the lateral epicondyle.

Of 16 injections in 14 patients, distinct improvement was obtained in 4 who had been treated with hydrocortisone and in 3 patients treated with procaine. No change was noted in 5 patients who had been treated with hydrocortisone and in 4 patients treated with procaine. Thus, the effect of the two substances seemed about the same. It is suggested that the reaction of hydrocortisone and procaine is mechanical rather than specific. *—Edgar L. Ralston, M.D.*

Tennis Elbow: (Epicondylalgia Externa); Treatment with Hydrocortisone. C. E. Quin and F. A. Binks. *Lancet*, Lond., 1954, 2: 221.

Thirty-one patients with tennis elbow were treated with hydrocortisone, by local injection. The authors do not state whether the injection was made subperiosteally over the epicondyle, or into the joint itself. The usual dosage was 25 mgm. Relief was noted within 24 to 48 hours and in only 2 patients were any complications noted; these were of a minor nature. All but 5 of the patients were improved after the first injection. Relapse followed in only 4 patients. Of the 31 patients, 27 have remained symptom-free for at least a month. *—Edgar L. Ralston, M.D.*

Tennis Elbow; Treated with Hydrocortisone Acetate. A. H. G. Murley, *Lancet*, Lond., 1954, 2: 223.

The treatment of 37 patients with a typical tennis elbow is reported. Nineteen of the patients were treated with local hydrocortisone, 25 mgm., while the second group of 18 was treated with a similar volume of 2 per cent procaine. Those on hydrocortisone seemed to improve more rapidly and the improvement seemed to be maintained for a longer period of time. Relapse was seen in both groups, those in the hydrocortisone group usually responding to a second injection. *—Edgar L. Ralston, M.D.*

Idiopathic Scoliosis; the Prognosis, Diagnosis, and Operative Indications Related to Curve Patterns and the Age at Onset. J. I. P. James. *J. Bone Surg.*, 1954, 36-B: 36.

This clear, concise, and informative article divides spinal curvature into various components. These individual curves develop at definite age periods and a definite prognosis is associated with each. The four major patterns are lumbar idiopathic scoliosis, thoracolumbar idiopathic scoliosis, thoracic idiopathic scoliosis, and cervicothoracic idiopathic scoliosis.

By analyzing these curves and their various behavior patterns closely, the author is able to state that the lumbar and perhaps the combined thoracic and lumbar curves never need correction, although fusion may be indicated for relief of pain. The thoracolumbar curve rarely requires fusion, but in true thoracic scoliosis, with its onset in adolescence, the percentage of patients requiring treatment is 80 or more. The author also makes the statement that by considering the curve pattern and the age of onset, the prognosis can be predicted with a reasonable degree of certainty, and a therapeutic program can be outlined.

—E. W. Johnson, Jr., M.D.

Osteomyelitic Foci of the Neck of the Femur (Focolai osteomielitici del collo del femore). L. Bitossi Coronedi. *Arch. Putti chir. org. movim.*, 1953, 3: 45.

This interesting study goes into great detail on the location, spread, and complications of osteomyelitic foci located in the neck of the femur and upper shaft. Particular stress is laid on what Koenig called synovial coxitis from a nearby primary focus in the head in contrast to the acute and primary septic arthritis.

Foci in the head itself are rare and the foci in the acetabulum hardly ever give rise to a diffuse osteomyelitis of the hip. There remain, then, the foci of the neck of the femur which are the topic of this study. The reason for their greater frequency lies in the circulation; the author distinguishes the following localizations:

1. Territory of the inferior (medial) cervical arch
2. The territory of the superior arch
3. The territory of the base of the neck (bulbometaphysial)
4. The subtrochanteric territory
5. The intermediate metadiaphysial territory
6. The diaphysial territory

These areas are defined on the basis of an anatomical study of the arterial supply of this region by Logroicino (1934).

1. *The foci of the inferior cervicodiaphysial arc* at the inferior border of the neck and above the lesser trochanter produce an early periosteal reaction, dense and compact, which form presents a potent obstacle against perforation into the joint. Because of this strong periosteal reaction it may be difficult to make out the rarefied area of the osteomyelitic focus in the roentgenogram. Also as the result of this reaction the focus may appear farther away from the contour and more in the depth, but closer study will reveal the appositional periosteal character of the contour line. Notwithstanding the marked periosteal activity, this type of foci entails great danger of penetration into the joint cavity.

2. *The juxtaepiphysial foci of the superior cervical* (lateral) *contour* are in a zone nourished by vessels which run along the superior contour from which they enter into the epiphysis. Here is noted the absence or scarcity of periosteal reaction. Articular complications are frequent and because of the vicinity of the growth plate, growth irregularities are observed. These foci are less frequent than those of the inferior arc, but share with them the danger of penetration into the joint. They are difficult to reach operatively.

3. *The bulbometaphysial foci* are relatively frequent and deeply seated in the spongiosa of the base of the neck. They are not easily visualized in the roetgenogram, and periosteal reaction, considering the deep location of the focus, appears late. There is marked peripheral reaction in the form of sclerosis. These foci are less dangerous, being deep-seated, but they spread toward the head, and produce diffuse involvement of the entire neck. Their localization makes them surgically accessible.

4. *The subtrochanteric metaphysial foci* are located deep in the mass of the trochanter near the anterior or posterior surface. They are not likely to penetrate into the joint and they present a precise indication for timely surgical interference.

5. *Diffuse and reactivated foci* appear as diffuse alterations of the trabecular structure of the entire neck, either primary or as a result of reactivation, and spread from primarily discrete foci. In both cases there are marked signs of reaction. Here the differentiation from invasive tumor is not always easy. Reactivations occur also in old chronic osteomyelitis to produce diffuse infiltration, and the very extension of the disease makes radical operation extremely uncertain. In the secondary, recrudescing type, the operative indication depends on the integrity of the joint.

Whether the initial stage is acute with violent pain or subacute, a constant sign is the articular reaction and the functional limitation resulting from it. The focus is separated from the joint only by a slender osseous wall which permits, if not passage of bacteria, at least transudation of inflammatory exudate. In a later stage the general symptoms and, especially, the pain abate. This is the phase in which x-ray evidence of the foci appears. In the earliest stages the foci represent areas of translucency. Once visible, at about 30 days after infection, their outlines are blurry. These foci may also include small visible sequestra. The periosteal reaction, always present, appears in one form or another. If the focus lies high, mediocervical, or juxtaepiphysial, the reaction is sleevelike and one sees the bone opposition most marked at the lower inner contour of the femoral neck, that is, on the concavity of the cervical curve. It seems that nature thereby provides a reinforcement of the weight-sustaining medial portion of the neck. When the focus lies more distally, the reaction is situated lower at the medial neck contour and may extend to anterior or posterior intertrochanteric lines. Periosteal reaction appears early, proceeds rapidly, and may entirely overshadow the underlying focus. There follows now a second stage of the condition, definitely chronic, which is characterized by both destructive and reactive phenomena.

Functional limitation has become stationary, or often even increases, but these increases are on physiologic rather than on anatomic grounds. At this time perifocal reaction is added to the periosteal reaction, ever increasing around the focus. But the latter may reach the joint cavity by extension, producing a new acute stage. However, as the clinical and roentgenological picture becomes stabilized, the last and chronic stage sets in, and in this stage there is no increase in temperature and but little pain. By this time the invaded joint may have gone on to ankylosis, but in contrast to tuberculosis such ankylosis does not mean the end of the inflammatory process. Even when there is solid fusion between the head and the acetabulum, new inflammatory foci may develop and lead to exacerbations of the clinical symptoms, pain, and temperature. The zone of rarefication appears, the periosteal reaction extends for a long distance, and new foci may join together to produce a diffuse inflammatory infiltration.

Of the conditions which may erroneously be diagnosed as osteomyelitis, the author mentions tuberculosis, tumors, and lues, the first being confused most frequently. In acute septic arthritis, the characteristic symptoms are dramatic, especially the pain. In the subacute forms differentiation from tuberculosis is more difficult. Osteomyelitic pain is more constant, and nocturnal. In initial tuberculosis there is the contracture, not often seen in osteomyelitis. The administration of penicillin is of diagnostic value in osteomyelitis. Multiple foci seen in the roentgenogram definitely suggest osteomyelitis. Of great importance is the periosteal reaction; it is massive, begins early in osteomyelitis, and increases rapidly; it is scarce or absent in tuberculosis. In the late phases the differential diagnosis is not difficult because tuberculosis does not produce the great changes in the bony structure. In tumors, the history and absence of temperature are important, both in benign lesions, such as cysts, and in malignant ones, such as Ewing's tumor. Luetic lesions have a marked sclerosing aspect, but serologic examination should never be overlooked.

Before the appearance of roentgenologic changes treatment is conservative, that is, it consists of rest, immobilization, and the use of penicillin. This initial phase is not fixed but varies from case to case, being determined by the roentgenologic appearance of the focus. When changes appear, surgical treatment must be considered. When any doubt as to tuberculosis exists, one should wait. One should also hesitate when the removal of the focus entails any danger to the joint. When the focus is well outlined, well localized, and accessible, surgical intervention should be prompt. It must be absolutely extra-articular.

The author uses two types of approach: one is the anterior, between the tensor and the gluteus, and the other is lateral, along the lateral aspect of the greater trochanter. The latter can also be used for multiple juxtaepiphysial foci. Careful attention must always be given to the articular cavity. The lesion must be carefully drained. The subsequent treatment rests largely upon the administration of antibiotics. The main principles are absolute sparing of the acetabular cavity, conservation of the static efficiency of the neck of the femur, accurate cleaning, and wide opening of

the foci. The difficulties are decreased if there is already an ankylosis.

Treatment, however, is not always surgical. The prospect of succeeding with antibiotics alone is best in the period before roentgenologic evidence is present and gradually diminishes with the progression of the disease, while, on the other hand, the prospect of surgical treatment increases. The latter has its best indication in the short period during which the lesion appears clear and well demarcated in the roentgenogram. In frankly chronic cases surgery is necessary, but it has only the value of symptomatic treatment.

—*Arthur Steindler, M.D.*

Popliteal Cysts (La cisti del poplite). J. L. OGGIONI. *Arch. Putti chir. org. movim.*, 1953, 3: 413.

DURING the period between 1947 and 1951 the author observed 13 cases of popliteal cysts. Operations were performed in 11 of these. The first account of this condition goes back to 1840 when Adams reported it as a tumor. It was named Baker's cyst in 1877, after William Baker, who, following studies on the cadaver, reported 8 cases of swelling in the popliteal fossa; 2 additional cases were reported in 1885. Baker found that these cysts were simply herniations of the posterior wall of the joint, due to osteoarthritis.

The author's series is of interest because of the use of arthropneumography which demonstrated the communication of the cyst with the joint.

In 1938, Haggart found that most often the cyst represents an enlargement of the bursa between the medial head of the gastrocnemius and the semimembranosus muscles, and directly connected with the joint by means of a pedicle. The walls of the cyst are of the same formation as the articular synovia, with signs of chronic inflammation. It would seem, therefore, that the cyst is caused by an inflammatory irritation, and the chronic changes of rheumatoid arthritis developing in the joint.

So far as the present communication is concerned, Wilson, Eyre-Brook, and Francis, in 1938, reported their findings in a complete study of this bursa on 30 cadaver specimens (22 operations). They found communication with the joint in 15, and doubtful communication in 5. Meyerding and Van Demark who operated on 15 patients in 1943 found the capsule very much thinned posteriorly, along the lateral margin of the medial condyle of the femur, a condition which Shands, Meigs, and Huggins ascribe to congenital weakness of the joint capsule. Trauma was found to be a factor in 7 of the 15 cases reported by Meyerding and Van Demark. According to the author, the posterior synovial wall of the joint acts much like the internal orifice of the inguinal canal, and as a result of trauma or rheumatic inflammation the articular fluid may easily extend into the bursa. The patient begins to notice some difficulty in movement of the knee, with gradually increasing pain in the popliteal space.

The diagnosis is relatively simple. There is a round, well outlined swelling, not particularly sensitive to palpation, no reactive signs, and some pain on flexion and extension. Some quadriceps atrophy. The x-ray shows a round shadow above the gastrocnemius head. All authors agree on the advantage of the use of contrast media, for which uroselectan B was chosen in doses somewhat greater than those for the visualization of the menisci. By this method the communication of the cyst with the joint cavity can be easily demonstrated. Often the opaque fluid fills the cyst, thus showing its entire outline. The lateral picture is of greater value because it differentiates the meniscus lesions and shows the extension from the joint cavity into the cyst. All authors agree that the indication is operative except in cases in which there is a contraindication on general grounds.

The operation is simple: a popliteal incision is made medial to midline, slightly oblique downward. The superficial fascia is incised and the cyst, which appears between the medial head of the gastrocnemius and the semimembranosus, is exposed. The cyst is freed from adhesions down to its pedicle; the latter is fixed by a hemostat and the cyst is removed. Following the operation the patient wears a knee splint for 10 to 15 days, then physiotherapy is begun.

Having found communication between the cyst and joint so frequently, the author believes it to be the normal condition. Only by arthrography with a contrast medium can one decide whether or not there is a popliteal cyst, i.e., a true herniation of the joint. On these terms the author defines the enlargement of the bursa between the gastrocnemius and semimembranosus muscles as a true cyst developing frequently after trauma. Surgical intervention is the only treatment considered. The author cites 9 cases.

—*Arthur Steindler, M.D.*

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

The Traumatic Anatomy and Treatment of Acute Acromioclavicular Dislocation. J. S. HORN. *J. Bone Surg.*, 1954, 36-B: 194.

FOLLOW-UP studies of the conservative treatment of patients with acromioclavicular dislocation revealed that those engaged in heavy manual labor often complained of pain and weakness of the affected shoulder. This was manifested in lifting a loaded shovel or in raising or carrying a heavy object held in the hand. Clinical examination suggested that the symptoms arose from damage to the deltoid and trapezius muscles.

To determine the precise nature of the lesion, a policy of surgical exploration at the acute phase was instituted and the findings were so uniform that there was scarcely any variation in 9 patients. The deltoid had been avulsed from the outer end of the clavicle for a distance of 2 to 5 cm. In some cases the overlying fascia was intact. The trapezius had been split in the direction of its fibers which are nearly horizontal in this region. This caused a gap between the superior segment of the muscle which gains insertion through the clavicle, and the segment immediately below which inserts on the spine of the scapula and the acromion. The deep fascia was usually rolled over the free edges of the split. The outer extremity of the clavicle lay free under the skin and the acromioclavicular capsule was completely disrupted. The meniscus, when present, remained with the acromion but

was often partly extruded. In four cases the lower free edge of the split trapezius lay across the acromion and prevented closed manipulative reduction. In all but one case, both conoid and trapezoid ligaments were completely ruptured.

The author suggests that the essential difference between subluxation and complete dislocation of the acromioclavicular joint may be that in the former only the ligaments are torn, and in the latter the muscles of the shoulder girdle remain intact and prevent wide separation of the clavicle from the acromion. The author believes that the space between trapezius and clavicle fills with scar tissue which is subjected to stretching and is the source of persistent pain and weakness.

Treatment should include full surgical exploration. The coracoclavicular ligaments are sutured but not tied until a strong suture can be passed vertically through the clavicle and acromion, to reduce the dislocation. The split in the trapezius is closed and the avulsed segment of deltoid is fixed to the clavicle. The arm is bandaged to the side for 6 weeks and thereafter active mobilization is encouraged. The patients regained full power and none complained of pain, but roentgenologic follow-up showed that when wire sutures had been used they were found to have broken shortly after resumption of activity, and slight subluxation of the acromioclavicular joint was present after the wires had broken. This displacement was not detectable clinically and was asymptomatic. The author believes it is the result of the ligaments having healed with some lengthening.

—*Norman J. Rosenberg, M.D.*

Selection of Skin Incisions in Surgery of the Hand (La scelta dell'incisione cutanea nella chirurgia riparatrice della mano). F. Fusi. *Arch. Putti chir. org. movim.*, 1953, 3: 283.

In 1914 Kanavel, in his monograph on hand infection (Philadelphia: Lea & Febiger, 1941), established the concept of tendon sheath and palmar thenar spaces in relation to drainage and specified the suitable skin incision. A good review of this monograph was written by Handfield-Jones (*Surgery of the Hand*. Baltimore: Williams & Wilkins, 1940).

The incisions used for drainage of the tendons and palmar spaces which do not respect the natural creases lead to irreparable scar contractures. The author, therefore, recommends that the skin incision meet the following requirements: it must give sufficient exposure; it must respect the neurovascular bundles, lymphatics, and tendon sheaths; it must reduce the visibility of the scar and, particularly, must not cross natural creases. It must follow the lines of the flexion creases strictly or be placed in so-called neutral zones where the gliding movement of the skin is minimal, for instance, in the lateral sides of the fingers or in the ulnar border of the hand. Sometimes a composite incision, curved or S or Z shaped, must be used when a crossing of the creases is unavoidable.

Specifically, the incisions are as follows:

Hand. For removal of small cysts or foreign bodies of the fingers, the incisions should be parallel to the creases. For the tendons, lateral incisions, either the dorsolateral of Bunnell (*Surgery of the Hand*. Philadelphia: J. B. Lippincott Company, 1948) or the dorsovolar of Koch (*Surg. Gyn. Obst.*, 1944, 78:9) and Mason (*Surg. Clin. N. Am.*, 1939, 19:227) are used. According to Bunnell the approach to the deeper structures of the fingers should be strictly dorsolateral because a volar lateral approach leads directly into the neurovascular bundle. The only inconvenience is hemorrhage from the smaller branches of the digital arteries. The incision used by Koch and Mason is more volar in relation to the neurovascular digital bundle. There is usually less hemorrhage, and by retracting the bundle one gains a better view of the flexor surface of the finger. The author's choice is the dorsolateral approach of Bunnell. Recently, MacIndoe (*Proc. R. Soc. M.*, 1950, 34: 56) proposed a short, central volar incision followed by a Z-plasty for the removal of the digital prolongation of strands in Dupuytren's contracture. The incision offers an excellent exposure for the removal of such fascial strands. In the dorsal region of the fingers the incisions should be transverse to spare the venous net and the dorsal cutaneous nerves. The complicated extensory apparatus of the fingers can be exposed by a lateral dorsal or a curved dorsal incision.

Thumb. The principles for incision are the same. To approach the long flexor tendon it is advisable to use an ulnolateral longitudinal incision. A radiolateral incision should run only distally from the metatarsophalangeal joint of the thumb, because more proximally it would cross the abduction creases of the thumb.

Interdigital folds. These should absolutely be avoided. If cysts or foreign bodies call for intervention, longitudinal incisions proximal to the webs should be used.

Palmar Region. The incisions should coincide with the skin lines and not cross them. The most easily injured anatomic structures are the proper digital nerve and the superficial palmar arch and its branches. A good incision is the curved one of Bunnell. It is useful for tendon sutures and tendon grafts at the palm, giving ample exposure and permitting suture of the lumbricalis over the point of tenorrhaphy. Bunnell also uses this incision for Dupuytren's contracture. The author found that when using this incision in cases of skin atrophy at the palm necrosis of the flap edges develops. For this reason he prefers the transverse incision along the distal palmar crease proposed by MacIndoe. For the removal of digital strands or nodes as in Dupuytren's contracture he uses the combination of central longitudinal incision with Z-plasty.

Dorsal Region of Hand. In this region the rule not to cross the cutaneous creases does not apply so much, although a long dorsal incision leads to interruption of the rich subcutaneous vasolymphatic system, edema, and rigidity. Short longitudinal incisions, however, heal with minimal cicatrization. During the removal of cysts or tumors in this region when it is necessary to keep the metacarpophalangeal joints in extension to relax the margins of the skin incision, a hyperextension contracture of the metacarpophalangeal joint may easily develop. To avoid this it is best to use the primary skin graft so that the joint may be held in flexion.

Dorsal Region of the Wrist. Incisions should be transverse, paralleling the creases. A longitudinal incision produces keloids. In order to avoid injuring nerves and vessels during the removal of synovial ganglia it is advisable to use a tourniquet. This is also done in opening the synovial sheath of the abductor pollicis longus in De Quervain's disease. In the latter case the best approach is a short longitudinal incision paralleling the styloid process, immediately followed by a Z-plasty.

Volar Surface of the Wrist. This surface represents the transverse flexor sulci. The incision should always be transverse. Tying of the cutaneous veins is of no serious consequence. In lacerated traumatic lesions the author prefers the bayonet incision.

—*Arthur Steindler, M.D.*

Articular Transplants from Foot to Hand (Trapianti articolare dal piede alla mano). E. MARCER. *Arch. Putti chir. org. movim.*, 1953, 3: 276.

JUDET, in 1908, and shortly afterward Michon and Axhausen (Judet, H. *Crend. Acad. Sc.*, 1908, 146:600; Axhausen, G. *Arch. klin. Chir.*, 1912, 99:1), did their first work on complete articular transplants and on hemiarticularization on animals and reported brilliant results. In 1912 Lexer (*Arch. klin. Chir.*, 1909, 90:263) carried out the first transplantations on the human being. He first did a hemitransplantation, substituting the proximal epiphysis of the tibia with one taken from a recently amputated limb. The functional results were fair and signs of aseptic necrosis and degeneration appeared in the transplant. Other transplantations were done by May (*Ann. Surg.*, 1942, 116:297) on the shoulder and knee with less favorable results. Recently, with the introduction of bone banks, the problem of articular transplantation has gained new importance. Extensive experiments were carried out by Herndon and Chase (*J. Bone Surg.*, 1952, 34—A: 564). These authors transplanted the complete knee joint in 129 dogs, and the clinical, radiologic, and pathologicoanatomic results were presented to the American Association of Orthopedic Surgeons. From all these reports the author believes that the indications for articular transplantation must still be confined to narrow limits.

Above all, he believes that only the smaller articulations should be considered. Better attachment is possible and there is less degeneration and necrosis. The donor should be the patient himself for foot to hand transplantation. Furthermore, only a complete transplantation holds out promise for functional repair or if a hemiarticular transplant (one of the joint constituents only) is done, it should be restricted to the nonweight-bearing joints, such as the shoulder. In the literature the only good functional results were obtained in the hand (Marziani, R. 33rd *Congr. S.I.O.T.*, Bologna, 1948). Particularly suitable is the metacarpophalangeal joint which can be substituted for by the metatarsophalangeal joint of the foot. It is best to use the third or fourth metatarsophalangeal joint.

In one case of a child of 9 with destruction of the distal epiphysis of the fifth metacarpal, the author performed a hemiarticular transplant together with the capsule which he sutured in collarlike fashion to the metaphysis of the proximal phalanx in order to avoid any subluxation. The transplant was held to the remaining stump of the fifth metacarpal by a Kirschner wire. It fused well, without dislocation or necrosis, but a stubborn rigidity remained evidently because the two articular surfaces (the one implanted, the other natural) did not adapt themselves to proper function.

For this reason the author discarded hemiarticular transplantation and in a following case used complete joint transplantation. The case was that of a boy of 12 years with pathologic fracture of the fourth metacarpal due to a large giant cell tumor. The entire metacarpal was removed with the tumor. For substitution the whole fourth metatarsal was taken, together with the metatarsophalangeal joint and capsule and a portion of the first phalanx of the fourth toe. This transplant was rotated 180 degrees because movement at the metatarsophalangeal joint is chiefly dorsalward while at the metacarpophalangeal joint it is directed volarward. Part of the basal phalanx of the fourth finger was then removed and the uncinate and the bases of the third and fifth metacarpals were freshened to facilitate the attachment of the transplant. Retention of the implant was accomplished with a Kirschner wire run through the basal phalanx of the fourth finger and then through the transplant, and was then left sticking out at the distal end for future removal. The wire was kept in place for 20 days, and after 30 days moderate mobilization was permitted. The result was perfect.

The author thinks that only the whole joint transplant assures success. This applies particularly to the small nonweight-bearing joints. Whether bank bone can be used is questionable. It is possible that fresh homogenous transplants may be used. The author is opposed to the use of bone bank bone for this purpose. While the bony substance may be well preserved, the soft tissue, synovia, capsule, and ligaments rapidly lose their functional qualities.

—*Arthur Steindler, M.D.*

Finger Flaps. O. W. WICKSTROM and B. E. BROMBERG. *Plastic and Reconstr. Surg.*, 1954, 13: 481.

THE problem of full thickness skin coverage of the digits is most frequently encountered in traumatic injuries, but must also be considered in other conditions such as Dupuytren's or other contractures, malignancies, and congenital deformities. Mode, place, and extent of injury are significant with regard to the wound, while age, sex, marital and economic status, his handedness, and occupation are equally important in the treatment of the patient. The final decision is ultimately an individual problem dependent on a multitude of factors.

Split thickness skin grafts are of use for emergency coverage, while full thickness skin is used for definitive treatment. Although the latter requires a minimum of two stages, it can often be accomplished in less hospital and operative time than other supposedly lesser involved procedures. The most desirable source of tissue is from the lateral and dorsal surfaces of adjacent fingers. The exposed radial surface of the index finger is not used. The digital flaps are constructed somewhat larger than measured, and planned so that future scar

lines will be in areas where danger of linear contracture bands is minimized. They are kept within proper width-length ratios, and dissection is performed under tourniquet, to prevent injury to tendon sheaths and neurovascular bundles.

When finger flaps cannot be utilized, thenar and palmar flaps are available. There is danger that the scar in the palm may cause discomfort, but this had occurred in only one case. While all flap donor sites are usually split skin-grafted, palmar donor sites may be allowed to granulate in, occasionally with excellent results. Any combination of flaps may be utilized. They are severed and inset, with or without previous delay, in 10 to 14 days. Adhesive immobilization is all that is required.

The results of finger and palmar flap operations are excellent functionally and cosmetically. The flap resembles most closely the tissue being replaced, and both sudomotor function and astereognosis return.

Larger amounts of tissue may be required in some cases, as in extensive skin avulsions or prior to bone and tendon reconstruction. In such situations, abdominal single pedicle or tubed pedicle flaps are recommended, although they will later require defatting. Forearm flaps are difficult to immobilize, while the burying of digits in subcutaneous tunnels becomes a long and tedious procedure.

Five cases are reported and illustrated to demonstrate the different methods discussed.

—Carl Schiller, M.D.

Treatment of Meniscal Rupture of the Knee Joint; a Follow-Up Examination of Material in Which Only the Ruptured Part of the Meniscus Had Been Removed. TORLEIV AARSTRAND. *Acta chir. scand.*, 1954, 107: 146.

IN ANY consideration of the surgical treatment of ruptured menisci of the knee joint, the extent of surgery which should be performed is debatable. Those who employ complete excision of the meniscus are as emphatic in their stand as those who advocate excision of only the ruptured part. Removal of the torn portion of the meniscus would seem to be less traumatic to the joint, and to favor speedier recovery because the approach and the operation are performed through a relatively avascular part of the knee joint.

The author notes that Smillie, Mercer, Klapp, and Tavernier favor total excision of a ruptured meniscus because other tears may be missed if only partial removal is done and because incomplete excision does not allow for regeneration of the meniscus. On the other hand, by presenting 54 cases in which torn menisci of the knee were treated by excision of the torn portion only, the author hopes to resolve the argument regarding the extent of surgery necessary for a good result.

"Entirely satisfactory" results were obtained in 40 cases (87 per cent). Postoperative arthrosis was noted in 19 per cent of the total series. These figures compared very favorably with percentages from comparable series of cases in which complete excision of the meniscus had been done. Such possible consequences of partial excision as recurrence of the tear, postoperative joint instability, and postoperative synovitis were considered, but found not be increased in this series as compared to series in which complete excision had been done.

Although his series is too small and the period of observation too short, the author concludes that it does, nevertheless, point to the fact that excision of the ruptured portion of the meniscus is a worth-while surgical procedure. *—E. W. Johnson, Jr., M.D.*

The Compression Method of Key-Charnley in Resection of the Knee for Tuberculosis (Il metodo della compressione di Key-Charnley per la resezione di ginocchio nella tubercolosi). D. R. ZUROVAC and G. SENIS. *Arch. Putti chir. org. movim.*, 1953, 3: 250.

IT IS ASSERTED that the fact that compression, rather than distraction, promotes osteogenesis was recognized by Wolff in 1892. It was in 1949 that Eggers, Shindler, and Pomerat confirmed this by their experiments on the skulls of rats, which showed that contact compression is important in stimulating osteogenesis and assuring bony union. Recently, published experiments of Gelbke (*J. Bone Surg.*, 1951, 33-A: 947) demonstrated that permanent compression inhibits longitudinal bone growth without causing a compensatory increase in width and that this is caused by the arrest in the proliferation of the epiphysial cartilage (a fact which was shown long ago by Scaglietti in his experiments on the pressure effect on the epiphyses of young animals); further, that permanent traction does not increase enchondral bone growth, and that such changes in enchondral growth as are produced by mechanical forces are, within certain limits, reversible (also established by Scaglietti long ago).

The authors, on the strength of these facts, followed in the steps of Key (1932) with compression arthrodesis of the knee, and in the steps of Danis (1945) who had considerable success with axial compression for the consolidation of fractures, calling it "osseous fusion per primam." Charnley, in 1948, took up the principle for the resection of the knee, using the following technique: after resection of the articular ends across a transverse incision, the wound flaps are readjusted for the insertion of the nails. The first, or lower, nail is inserted through the proximal metaphysis of the tibia, and the second, or upper, is inserted parallel to the first, through the distal metaphysis of the femur. The same Key Charnley technique was used by Parisel (*Acta Orthop. Belg.*, 1940, 6: 327) in 7 cases, and by Morris and Masiman (*J. Bone Surg.*, 1951, 33-A: 982) in 24 cases of which 5 were tuberculous.

In the Istituto Porto Potenza 24 patients were operated upon in the last 6 years, 12 of them in the last 2 years by the Key Charnley technique. In the 12 earlier cases in which the conventional technique of resection was used complete fusion was not attained, as evidenced by the roentgenogram, in less than 3 months, during which time a hip spica had to be worn and after this a long leg cast for another 3 months. The other 12 patients operated upon in the last 2 years were 4 children and 8 adults. The author used gauze soaked with a coagulant and streptomycin after removal of the synovia for local hemostatic and antibiotic action, especially for the upper nail; no such precaution was necessary for the lower nail which did not touch the synovial cavity; however, the gauze was

applied from the lateral to the medial surface to avoid injury of the external popliteal nerve. In children the resection was flat, while in adults it was cuneiform in the sagittal axis. Eventually the foci were evacuated with the curette. After wound closure streptomycin was again used with the dressing and the limb was immobilized with a simple long leg cast including the foot. This cast was kept on for 3 weeks in children and 4 weeks in adults. After this period there was clinical ankylosis in every case. In the roentgenogram the ankylosis was complete throughout the entire depth in the children; in the adults with cuneiform arthrodesis ankylosis was complete only in the posterior half which bore the most pressure. There was never any sinus formation. After removal of the leg cast a plaster splint was applied, in which the patient gradually took up weight bearing which was always painless.

The advantages of this operation are as follows: perfect adaptation and contact of the resection planes is obtained; the compression factor accelerates ossification; the patient wears only a long leg cast instead of a hip spica after operation and therefore recumbency is eliminated; weight bearing is started after 1 month, which with the old method was not possible before at least 3 months. —*Arthur Steindler, M.D.*

FRACTURES AND DISLOCATIONS

Isolated fracture of the Small Tuberosity of the Humerus (La frattura isolata del trochine). Antonio Mignogna and Eugenio Jannelli. *Riforma med.*, 1954, 68: 68.

Two instances of fracture of the tuberculum minus of the humerus are reported.

The first case was that of a 30 year old psychotic patient who, 4 days previously, had undergone shock treatment for a depressive psychosis. When she recovered from the period of unconsciousness, the patient noted pain in the shoulder on the right side. The pain was accentuated with movement of the shoulder joint, especially with the movements of external rotation and of abduction of the right arm. The pain did not decrease in the succeeding days, which made it necessary to maintain the arm in a position of abduction against the thorax. There was pain on pressure over the anterior margin of the deltoid muscle. Passive movement provoked pain.

Roentgenologic examination in the anteroposterior projection did not disclose any changes; however, the projection of Didiée, with the arm in internal rotation and in 75 degree abduction, disclosed a fracture of the lesser tuberosity.

The second case was that of a 24 year old aviation pilot who, 10 days previously, had experienced a forced landing. At the moment of contact of the airplane with the ground, the pilot was projected forward suddenly. With the hand holding the stick, the muscles of the shoulder girdle were held rigid to reduce the effects of the anteropulsion of the body, and the effects of the propulsion resulted in the abduction and external rotation of the rigidly held arm.

Immediately after this incident the patient noted sharp pains in the region of his right shoulder, pains which slowly ameliorated in the succeeding days, but without disappearing entirely.

Passive movements of the right arm were practically normal with the exception of abduction and of external rotation, which movements were partially restricted and painful. Roentgenologic examination in the position of abduction to 45 degrees and of internal rotation disclosed a comminuted fracture of the tuberculum minus humeri.

The authors describe another projection which might be used in the roentgenologic demonstration of the lesser tuberosity. In this projection the arm is abducted as far as possible and in indifferent rotation. The plate is placed supraclavicularly and the tube is directed in such a manner that the incident ray bisects the angle between the long axis of the arm and that of the trunk. This projection may be resorted to when the Didiée method might be considered too painful.

Therapy consists in immobilization of the involved arm in a position of moderate internal rotation and abduction for about 4 weeks. This treatment may prove sufficient for reduction of the fracture, especially in those instances in which the displacement of the fragment is not extreme. Marked displacement tends to be prevented by the fact that the subscapular muscle, the agent of traction in these instances, is attached not only to the tuberculum minus but also to the shaft of the humerus immediately below the tuberculum, as well as to the articular capsule.

In the rare instances of extreme dislocation of the fragment, or in those instances in which the fracture is not reduced after a long period of time, an osteosynthesis by means of the ordinary nail of Codivilla or by means of the nail of Delitala is recommended.

In the 2 instances reported, closed reduction was attained. —*John W. Brennan, M.D.*

The Use of the Acrylic Head Prosthesis in High Fractures of the Femoral Neck. J. C. F. Cregan. *J. Bone Surg.*, 1954, 36-B: 411.

Sixty-five cases of medial fracture of the femoral neck treated by substitution of the head by an acrylic prothesis have been studied. In general, the long-term clinical results of prosthetic arthroplasty after fresh fractures have been disappointing. The method has given slightly better results in the treatment of old fractures. In view of the almost perfect results obtained after successful Smith-Petersen nailing in the presence of an adequate blood supply to the femoral head, it seems unjustifiable to abandon this principle for immediate substitution with an acrylic femoral head. Nevertheless, it is believed that an arthroplasty of this type is justified in fractures seen late, and in fresh subcapital fractures when the fracture is irreducible.

Patients with fractures mainly lateral to the midpoint of the neck of the femur have been treated by Smith-Petersen nailing, provided they were reducible; therefore, the present series contains only medial fractures and irreducible lateral fractures.

The technique of the operation and the postoperative management are described. The posterior approach described by Gibbon was advocated because there is less bleeding and no damage is done to the gluteus medius; the head of the femur lies more superficially in the incision, and is more easily reached. The author stresses the importance of placing the prosthesis in as valgus a position as possible. No dislocation

of the prosthesis occurred in 30 cases in which the plaster hip spica was utilized. The latter extended to the mid-calf and held the calf in medial rotation, 20 degrees of abduction and 30 degrees of knee flexion.

In 53 fresh fractures treated by immediate operation, the hip condition was found to be comfortable during the first year for weight-bearing, and the range of movement has, by the fourth month, reached at least two-thirds of the normal in all directions. The patient has usually used a cane outside, discarding it in the house, and walking with a slight limp but with little or no pain. During the second year some minor complaints have been the rule, such as aching in the hip, or disinclination to go shopping or to climb stairs in the house. During the third year, 85 per cent of the patients stated that the hip was painful to a greater or lesser degree. In 2 patients the prosthesis fractured spontaneously during the first year at the junction of the head and stem. The prostheses were excised and replaced with a corresponding loss of function.

From this study it seems that acrylic prosthetic arthroplasty has definite limitations in the treatment of fresh fractures of the femoral neck. The hip function, after the operation, has been sustained a little better in patients operated upon late than in those operated upon immediately, but in both groups a decline in the efficiency of the joint has been the rule. By the third year the neck has become absorbed and shortened to a variable extent in 79 per cent of cases and the hip has become painful.

In the small group of old fractures operated upon late as a secondary procedure, the range of movement has been slower to recover but hip function, once regained, has been maintained a little better (12 cases).

The new bone formation has been a common feature, occurring in the capsular attachments to the acetabular margins and the trochanteric regions, and sometimes in the gluteal insertion. It was present in 70 per cent of cases by the second year and in 92 per cent by the third year.

The alignment of the prosthesis has seldom remained constant. By the second year 36 per cent of the cases showed an increase in varus position, which rose to 80 per cent in the third year; the 10 cases, in their fourth year, all showed gradual varus alteration. In 2 patients acute painful episodes developed in the first year, because of a small fracture of the neck stump, with resultant varus deformity of the prosthesis.

A study of 8 patients with reasonable function persisting into the third year shows that some new bone formation has occurred in the capsule. The shortening of the neck has been minimal, and, in particular, the inferior border of the neck and the upper part of the calcar have remained intact. The bone in this region has evidently become denser and better able to stand the strain of weight-bearing. Nevertheless the presence of an intact neck stump seems to be no guarantee of long-term success.

Twelve cases were noted at operation to have either a displaced or undisplaced (unsuspected) V-shaped fracture of the inferior border of the neck extending into the region of the calcar. The results in these cases were among the poorest.

In view of the gradual deterioration that has been observed in the second, third, and fourth years, it seems that in most cases acrylic substitution as a primary operative treatment for this injury cannot be relied upon regularly to give a satisfactory hip, even in elderly patients who are unlikely to make great demands on it. —*C. Fred Goeringer, M.D.*

Treatment of Fractures of the Tibial Condyles by Active Movement Therapy. R. V. LINDHOLM. *Acta orthop. scand.*, 1954, 23: 320.

THE AUTHOR reports a case of medial fracture of the tibial condyle. The patient was treated at the clinic by early active movement in a balanced position of suspension. Good restoration of the tibial plateau by reposition, spontaneously occurring under treatment, was achieved with good mobility and a stable joint. The danger of prolonged immobilization in intra-articular fractures is stressed.

—*Daniel H. Levinthal, M.D.*

A New Method of Treatment for Fractures of the Calcaneus (Nuevo metodo de tratamiento de las fracturas del calcaneo). F. A. MANDRUZZATO and G. BRUNELLI. *Acta ortop. traumat. iberica*, 1954, 2: 41.

ALL pertinent details of fracture classification, choice of operative technique, and results obtained prior to the evolvement of the present operation here described were presented by Mandruzzato in a previous publication (*Acta orthop. Belg.*, 1951, 17: 220) and an excellent abstract of this article in English was written by Werner M. Solmitz in the *International Abstracts of Surgery*, 1952, 94: 392.

The fracture which involves only the epiphysis of the heel bone, i.e., it does not involve the supporting mass under the talus with its articular facets, is treated orthopedically. A cast is applied which is well padded under the arch of the foot; later the heel portion of the cast is cut away and a Kirschner wire is passed through the fragment of the calcaneal tuberosity which has been broken loose. The Kirschner stirrup is then maintained in traction by means of a metallic arch imbedded in the cast itself. After 20 days the cast is enclosed, including the wire, and left without traction for another 2 weeks. After the month has passed, a small cast is substituted and walking is permitted.

The fractures involving the region of the articular facets are now being treated by a new method. A specially constructed nail with a T-shaped cross section is introduced through a small incision in the midline over the tip of the heel bone (4 cm. in length), and passed (driven) through the prebored canal through the cortex and spongiosa of the calcaneal tuberosity-fragment to just under the supporting mass (the so-called thalamus). The handle to the nail, which is about 20 cm. in length, is then used as a lever; the apophysis is levered downward and inward (restoration of the angle of Böhler) and the mass is forced upward into its natural position. The nail is then driven clear in, so that the skin can be closed over it, traversing the mass and even on occasion penetrating into the subtalar joint (more of an advantage than a disadvantage), and even into the talus itself.

At the same time the attempt is made to correct the lateral spread of the fracture area, either manually or instrumentally. All manipulations are done under roentgen control. The nail itself is not straight but

presents a curve with the open side toward the shaft of the T; thus when the force of leverage is applied, the shaft of the T is the part of the nail which carries the burden, the two laterally projecting wings of the T merely getting a firm grasp in the spongioid tissues.

One week after this operation is done, a plaster cast is applied, and after 20 days the patient is permitted to walk about. After 50 to 60 days the cast may be removed and an orthopedic shoe prescribed.

Thus far only 10 patients have been treated by this surgical method (metallic osteosynthesis) and the time is too short for final evaluation of the results; however, the roentgenograms and the print on paper of the sole of the foot after healing shows that the deformities have been adequately corrected, even overcorrected in some instances.

—*John W. Brennan, M.D.*

ORTHOPEDICS IN GENERAL

Development of Progressive Changes in Muscles Paralyzed by Peripheral Nerve Injury (L'evolversi delle alterazioni regressive nei muscoli scheletrici umani paralizzati per lesione di nervi misti periferici). C. POGLAYEN. *Arch. Putti chir. org. movim.*, 1953, 3: 306.

THE LITERATURE on paralyzed muscles due to peripheral nerve injury offers only laboratory studies on animals. Secondary neurogenic muscle atrophy in man has been given little study. The author carried out his study on biopsy material. A nerve severed or constricted is no longer excitable; continuity, anatomic as well as physiologic, is essential. The author's material comprises 35 cases: 6 lesions of the popliteal nerve, 9 of the musculospinal nerve, and 20 of the common sciatic trunk. In the first group, material was obtained from the posterior tibial muscles from 4 months to 2 years after the injury. In the second group the common extensor muscle of the fingers was obtained from 5 months to 2 years and 10 months after the injury; in the third group the gemelli were examined from 3 months to 3 years after injury.

The investigation showed that the atrophic and degenerative changes vary according to the time interval. In all, the electric excitability was altered and the complete reaction of degeneration was present in all of the cases.

The first stage is one of atrophy lasting up to 6 months after the lesion. In the second stage (6 to 15 months following the injury) there is atrophy and degeneration. The muscle is reduced in volume in its transverse diameter. Macroscopically, it has a pallid pink color, in contrast to the reddish brown color of normal muscle. Yellowish gray streaks appear in it. In the third stage (15 months to 2 years) degeneration prevails. The muscle is atrophic and shrunken, has lost its natural firmness, and is friable. In the fourth stage (after 2 years) fibrosis occurs. There is marked loss of volume and it is not always possible to separate the muscle from the fibrous and fatty masses which surround it.

HISTOLOGY. *Stage of atrophy.* In this stage the diameter of the muscle fibers is unequal, longitudinal striation is preserved, and cross striation has disappeared. In transverse section the muscle fiber has lost its normal polygonal form. The fiber appears opaque with a tendency toward metachromasia. The larger fibers often present transverse clefts. The ground substance is hyalinized; there is vacuolization with amyloid and fatty degeneration. Slight longitudinal fissures divide the fiber in the fibrilli with signs of degeneration. The nuclei are large, ovoid, and pale; they seem to be more numerous and have a tendency to move toward the axis of the fiber. The blood vessels develop a thick wall which is chiefly constituted of muscle cells. The latter are arranged in two strata, one is internal and longitudinal and the other is external and circular. Nerve trunks show a marked hyperplasia of the connective tissue. The myelin sheath has disappeared and the axis cylinders become fragmented. Particularly in the perimysium externum one sees a more or less dense lamellar connective tissue develop with a few muscle fibers more or less atrophic and degenerated in the center.

Stage of atrophy and degeneration. This is an alternation of both processes. There is a variable thickness of muscle fibers, generally reduced; longitudinal striations are still visible, but transverse striation is absent. The nuclei of the sarcolemma increase numerically and are displaced toward the center. The fibers become undulated, the fibrilli tortuous, and the whole fiber is fragmented. Some of the fibers appear to be detached from their sarcolemma sheath. There are metachromatic phenomena, and the nuclei are increased in number and size. The reticular sheath of the muscle is particularly abundant; there is perifascicular and interfascicular hypertrophy. The histologic appearance of the blood vessels is similar to that in the previous stage. There is hyperplasia of the walls, almost entirely of the muscle tissue. The nerve trunks show hypertrophy of the connective tissue. The neuromuscular plates show dilated lymphatic vessels. No nervous elements are recognizable. The muscle fibers are in a state of combined atrophy and degeneration, different from fiber to fiber. One fiber may be completely substituted by fibrous tissue, while another may be in a state of hyaline degeneration.

Stage of degeneration. Atrophy is markedly advanced, but the process of degeneration prevails. Numerous fibers are in hyaline metamorphosis. In transverse section one finds albuminoid and fatty degeneration with foam-cell appearance in the center of the muscle fibers. There are, in fact, various types of cells invading the muscle fiber. Sarcolytic cells are formed by the disintegration of the contractile substance, and the longitudinal section shows marginal nests of 8 to 10 arranged in a rosary which are filled with nuclei. Other fibers have completely disappeared. The vessels show progressive hyperplasia; the nerve trunks, while preserving their shape, show loss of myelin and of axis cylinders, and thickening of the Schwann's sheath.

Stage of fibrosis. The muscle has lost all its fibers, which are replaced by connective tissue. Only a very few atrophic fibers are found, and these represent small discs in which there are 2 or 3 nuclei. The contractile substance is almost entirely gone. Only the external sarcolemma tube remains, containing nuclei which show degenerative changes such as pyknosis and confluence. Both the perimysium externum and internum are hypertrophied. There is deposition of adipose tissue. The vessels show hypertrophic media.

The nerve trunks are transformed into tough fibrous strands by metaplasia of the elements of Schwann's sheath. Of the neuromuscular junctions nothing remains except the capsule and collagenous tissue. With the interruption of the nerve supply, voluntary contraction ceases and all muscle tone disappears. There is degeneration. The cause of this is not inactivity; the latter produces a loss of muscle mass, but the muscle does not degenerate from inactivity alone and therefore preserves its characteristic properties. Nerve interruption also produces trophic, vasomotor, pilomotor, and secretory changes. Nor can the loss of weight and of contractility be prevented by physiotherapeutic means. From the trophic nerve centers of the medulla come the nutritional changes. It is for this reason that the striated muscle degenerates.

Perroncito, Boecke, and Kure have shown that aside from the myelinated nerve fibers in the muscle, there are also nonmyelinated, supposedly sympathetic fibers. Each fiber therefore receives innervation from the vegetative as well as from the somatic fibers. However, Bottazzi and many others maintain that the sympathetic fibers are exclusively vasomotor. Be that as it may, the motor nerve interruption produces immediate hyperemia. In all of these four stages the atrophic-degenerative changes develop very irregularly; one has the impression, as Meyenburg terms it, that each fiber takes its own independent course. The connective tissue of the internal and external perimysium does not remain inert; it proliferates and pushes on between the muscle fibers, which later become more and more reduced while their sarcolemmas gradually increase. The opinion that this newly formed connective tissue derives, aside from perimuscular and intramuscular collagen fibers, also from the muscle substance itself by way of metaplasia cannot be set aside entirely. It also seems that the vasomotor changes which follow the denervation are responsible for the metamorphosis of the denervated muscle. Finally, the thickening of the vessels may compensate in part for the loss of tone of the paralyzed muscles which no longer can act as blood pumps, and the sympathetic denervation may be in relation to an anoxic stimulus. The neuromuscular junctions also follow the same atrophic-degenerative cycle which the muscles do.

There are certain practical inferences to be drawn. The muscle fibers, according to Bizzozzero, are permanent and static structures. They do not increase in numbers with age but remain numerically stationary. Therefore, contractile elements cannot be replaced by newly formed fibers. It is necessary, therefore, to provide nerve stimulus to the muscle fibers before they disappear altogether under the progressive scheme of degeneration. If during this period one succeeds by nerve suture or neurolysis to restore nerve function, there exists the probability of muscle regeneration. Even though theoretically the time of nerve repair may not seem of great importance, it is eminently so from the practical standpoint. In fact, as atrophy and degeneration of the muscle proceed, muscle regeneration may become greatly hindered. Therefore, it is advisable not to let too long a time pass before intervention is undertaken on the nerve trunks. Each month that passes decreases the chances of repair. When the third stage of the prevailing degeneration is reached, recovery may be insufficient for practical use.

—*Arthur Steindler, M.D.*

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Transplantation of the Saphenous Vein for Post-phlebitic Stasis. RICHARD WARREN and THEODORE R. THAYER. *Surgery*, 1954, 35: 867.

TRANSPLANTATION of the saphenous vein into a surgically created muscular compartment of the thigh was carried out in 14 patients. In one-half of these the saphenous vein was freed and transplanted to the muscular compartment only; whereas, in the second half the same transplantation was accomplished but, in addition, the vein was divided at the knee and an anastomosis was performed between the proximal segment of the saphenous vein and the distal segment of the divided popliteal vein. If an anastomosis was carried out, the distal end of the saphenous vein was either simply ligated (2 cases) or the distal end was stripped or removed by direct excision (5 cases). The muscular compartment was created by an incision between the adductor muscles of the thigh and the extensor muscles of the knee. In later operations the sartorious muscle was divided, such division allowing a more complete transplantation of the vein. A regional heparinization was used in all 7 patients in whom anastomotic procedures were carried out.

Ten of the 14 patients demonstrated clinical improvement in that the ulcers healed or improved, or evidences of dermatitis and/or edema diminished. No patient was cured. The good results were distributed evenly between the two types of operation. In general, the changes in walking venous pressure correlated well with the clinical improvement. In 7 instances, the changes in walking pressure showed improvement. Preoperative and postoperative phlebograms were carried out in all instances. The transplanted vein in the 7 patients who had only saphenous transplants was readily visualized as being patent. In only one of those instances in which anastomosis was carried out could the transplant be said to be definitely patent. In 2 of the 14 patients there were major complications: necrosis of the medial skin flap in 1 patient and sudden acute worsening of the evidences of deep phlebitis in another.

Future studies should include the application of a similar type of procedure to the thigh primarily, the evaluation of the valves in the saphenous system, and the possibility of transplantation of healthy valved veins from elsewhere in the body.

—Jerry A. Stirman, M.D.

Surgical Management of Ulcerative Stasis Disease of the Lower Extremities. ORMAND C. JULIAN, WILLIAM S. DYE, and JOHN SCHNEEWIND. *Arch. Surg.*, 1954, 68: 757.

THE UNIFORMITY of location of serious stasis changes leading to ulceration of the lower extremity suggests an anatomic peculiarity in the regions. The factor responsible is probably the presence of incompetent perforating veins between the superficial and deep circulations in this area.

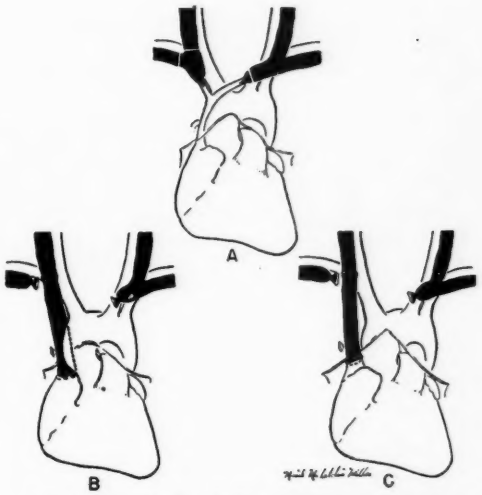


FIG. 1 (Scannel, Shaw). Diagrams to demonstrate the pathological problem (A), and the method of solution (B and C). In Case 1 a free vein graft was placed between the right internal jugular vein and the intrapericardial portion of the superior vena cava (C). In Case 2 the graft was placed between the internal jugular vein and the right auricular appendage.

Severe and often irreversible changes occur in the skin and subcutaneous tissue of the stasis area accompanying the ulcer.

Removal of both factors by radical excision of the stasis area and replacement by split-thickness skin graft has been accomplished in 41 patients whose response to the treatment has been followed for periods up to 5 years.

The clinical results are acceptable in this stubborn disease, but the not infrequent failures show the need of additional armamentaria which may well be femoral or popliteal vein ligation.

—John J. Maloney, M.D.

Surgical Reconstruction of the Superior Vena Cava. J. GORDON SCANNELL and ROBERT S. SHAW. *J. Thorac. Surg.*, 1954, 28: 163.

TWO UNUSUAL CASES of obstruction of the superior vena cava were treated successfully by surgery. The first patient unfortunately died on the eighth postoperative day from a mediastinitis secondary to a dehiscence of the incision. However, at postmortem examination the vein graft, in spite of the mediastinal sepsis, was perfectly patent. The second patient showed general clinical improvement 1 year postoperatively.

Such cases of superior vena cava obstruction are rare. The obstruction is corrected by a free vein graft, which can be used successfully in cases presenting a

benign or stationary basis for obstruction of the superior vena cava. —*John E. Karabin, M.D.*

BLOOD; TRANSFUSION

Determination of the Survival of Transfused Red Cells by a Method of Differential Hemolysis. THOMAS H. HURLEY, RUSSELL WEISMAN, JR., and ANGELA E. PASQUARIELLO. *J. Clin. Invest.*, 1954, 33: 835.

THE technique of differential agglutination of red cells has been widely used to measure the life span of red cells following transfusion. The technique of differential hemolysis was investigated by these authors as a possible alternative to this method in an attempt to separate more easily the surviving donor cells from those of the recipient.

Differential hemolysis is employed in the study of the survival of red cells in a manner similar to differential agglutination. Compatible but antigenically distinct red cells are introduced by transfusion into the circulation of a suitable recipient. The survival of these transfused red cells can then be followed in their life span in the recipient by taking samples of blood containing the mixed cell population, eliminating the cells of the recipient by exposing the mixture to the appropriate hemolytic antiserum, and counting the remaining number of donor cells which are not subject to hemolysis.

The method of differential hemolysis is different from that of differential agglutination in that hemolysins are used instead of the corresponding agglutinins in the separation of the mixed cell population. Since anti-A and anti-B are the only isoantibodies which occur in the form of potent hemolysins the technique is limited to transfusions within the ABO system and, unlike the method of differential agglutination, cannot be used in studies dependent on the M, N, or D antigens. The ability of the hemolytic sera employed to hemolyze all but a very small fraction of the cells of the appropriate blood group is obviously of importance if the method is to be reliable. It was found that even the most potent hemolytic antisera did not lyse all the cells in any instance, and that a small number of unhemolyzed red cells always remained. In any prospective recipient for a study of cell survival it is necessary, therefore, to determine the number of his cells per millimeter which are not hemolyzable by the hemolytic antiserum to be used in the study. This number, which corresponds to the unagglutinable or blank count in the method of differential agglutination, is referred to as the blank count. If the method of differential hemolysis is to be reliable in the estimation of the survival of transfused cells the blank counts of any hemolytic antisera used must conform to the specifications established for satisfactory antisera in the method of differential agglutination. Accordingly, the blank count must be low. About 20,000 cells per millimeter are usually regarded as the upper limit permitted. Also, the blank count should not vary significantly on the storage of the serum for periods of at least 5 months.

The method was used on 19 subjects and the results were fairly constant. The immunologic details are presented, as well as several charts and graphs to show the average length of time of survival of the transfused red cells. In general, a disappearance of practically all of the cells was noted by 120 days following the transfusion. In practically all cases there was a gradual diminution in the number of circulating donor cells as the study progressed, at 10 day intervals following administration of the blood.

—*Matthew H. Evoy, M.D.*

LYMPH GLANDS AND LYMPHATIC VESSELS

Lymphogranulomatosis Benigna; a Clinical and Histopathologic Study of Its Relation to Tuberculosis. LENNART ZETTERGREN. *Acta Soc. med. Upsaliensis*, 1954, Supp. 5.

LYMPHOGRANULOMATOSIS benigna refers to a syndrome described in 1914 by Schaumann, and characterized by bilateral pulmonary lesions, generalized swelling of the lymph nodes, and frequently a low sensitivity to tuberculin. This is recognized in the United States as sarcoidosis with attendant additional findings. Microscopically, lymphogranulomatosis benigna is characterized by sharply defined foci of epitheloid and giant cells, with caseation occurring rarely. Fibrous induration develops. Schaumann, in his description, did not discuss the histologic differential diagnosis between this syndrome and the forms of tuberculosis which German workers in particular call atypical, and the best known of which is the large-celled hyperplasia described by Ziegler. The present investigation aimed for a decision between lymphogranulomatosis benigna and tuberculosis, with special reference to the Ziegler form of tuberculosis.

The present study is described in a 180 page monograph translated by Dr. Ann Synge. There is included a detailed historical survey, a description of the clinical observations, the bilateral hilar lymphoma syndrome, the histopathology, and the various theories of its etiology. Four chapters are devoted to the author's investigations, with a discussion of the problem, material, and methods, and 2 series of cases. One hundred and eight case reports are included.

It is the author's conclusion that the chronic hyperplastic form of tuberculosis (Ziegler's large-celled hyperplasia) is not identical with lymphogranulomatosis benigna; however, lymphogranulomatosis benigna is also a form of tuberculosis, and the chronic hyperplastic form of tuberculosis is probably the intermediate form between classical tuberculosis and lymphogranulomatosis benigna. Except for the occurrence of asteroid bodies *only*, microscopic differences between the two seem to be differences in degree rather than in kind. A strong reaction by the reticuloendothelial system, causing rapid and complete destruction of the bacilli, gives rise to the lymphogranulomatous reaction. The pathogenesis of lymphogranulomatosis benigna is believed to be an atypical and slowly progressing form of primary tuberculosis.

—*Allan D. Callow, M.D.*

SURGICAL TECHNIQUE

OPERATIVE SURGERY AND TECHNIQUE; POSTOPERATIVE TREATMENT

The Role of Hibernation and of Decapsulation in the Treatment of Postoperative Anuria (Le rôle de l'hibernation et de la décapsulation dans le traitement des anuries postopératoires). E. LADURON and VILLE DE GOYET. *Acta chir. belg.*, 1954, 53: 351.

A 47-YEAR-OLD patient had undergone a hysterectomy for a fibromyoma. During the operation she received 500 c.c. of O Rh+ blood. During the first 3 postoperative days there was no output of urine. At the end of this time there were signs of pulmonary edema; rales were heard in both lungs and the cervical veins were distended; her pulse was 132; respirations were 48; blood pressure was 190 systolic and 120 diastolic. The patient was in poor condition. Hypothermia was induced with largactyl-phenergan and 12 liters of blood were withdrawn and replaced with 12 liters of type A Rh+ blood. Eight hours later her pulse was 128, respirations were 32, rectal temperature was 36.1 degrees C., blood pressure was 120 systolic, and 70 diastolic. The temperature was then lowered to 35.6 degrees C. with ice packs. After 24 hours of this treatment the pulmonary edema had subsided but no urine had been produced. Decapsulation of the right kidney was done. The kidney was very distended. Transrenal drainage of the kidney pelvis was established with use of a nephrostomy tube. In the following 24 or 30 hours, 420 c.c. of urine was passed by the right kidney and only 20 c.c. by the left. Thereafter large quantities of urine were passed by the right kidney. Several days later urine began to appear from the left kidney. Seven days after the decapsulation the output from the two kidneys was equal. Hypothermia was maintained for approximately 24 hours.

The cause of the anuria in this patient was obscure, but was thought to be on a reflex basis. The transfusion during surgery was not the cause, as was proven by subsequent tests of blood compatability.

—Frederick W. Preston, M.D.

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Infections Occurring During Chemotherapy; a Study of Their Frequency, Type, and Predisposing Factors. LOUIS WEINSTEIN, MARTIN GOLDFIELD, AND TE-WEN CHANG. *N. England J. M.*, 1954, 251: 247.

THE ADMINISTRATION of an effective antibiotic to a patient with an infectious disease, in addition to eliminating the causative organisms, produces an alteration in the composition of the bacterial population that normally inhabits certain tissues. This by-product of chemotherapy, while frequently of no importance, may on occasion be responsible for the superimposition of a serious infection on the one for which treatment was originally instituted. This complication occurred in 2.19 per cent of 3,095 patients studied.

The organs secondarily involved are most frequently the same as those affected in the primary disease. Superinfection occurs most frequently on the fourth or fifth day of treatment, and the organisms responsible are difficult to treat. The appearance of superinfection may convert a benign disease into a serious or even fatal one. This is most common in children under 3 years. Frequent bacterial studies to determine any change in the bacterial flora should be carried out.

The data obtained in this study emphasize the danger of antibiotic therapy in diseases that are not treatable, since superinfection, which may be a small risk in the untreated infection, may become a serious threat.

—Ely Elliott Lazarus, M.D.

Experimental Allergic Encephalitis in Animals, and Its Bearing Upon the Etiology of Neuroparalytic Accidents Following Antirabies Treatment in Man. GEORGE A. JERVIS. *Bull. World Health Org.*, 1954, 10: 837.

NEUROPARALYTIC accidents following antirabies treatment in man bear a striking similarity to experimental allergic encephalitis. In animals, allergic encephalitis has been produced by homologous or heterologous subcutaneous injections of brain material. The clinical manifestations vary somewhat from species to species, both in the time of occurrence and in the severity of the disease. The chief neurologic features are paralysis of the limbs, inco-ordination, impairment of ocular muscles, and convulsions. The chief pathologic features are perivascular infiltration of lymphocytes, leukocytes, plasma cells, microgliacytes, and demyelination of areas, occasionally with coalescence of these areas. Hemorrhages are frequent; the lesions are disseminated throughout the central nervous system. The nerve roots are occasionally involved. Although the etiopathogenesis of allergic encephalitis is not completely understood, the following features favor the antigen-antibody hypothesis: (1) the delayed development of lesions following injection of brain substance; (2) the enhancing action of "adjuvants"; (3) the depressive action of adrenocorticotrophic hormone in some animals and cortisone in others; (4) the depressive action of salicylate and p-aminobenzoic acid; (5) the occurrence of skin reaction to rabbit brain in guinea-pigs inoculated with rabbit brain, and to homologous brain in rabbits inoculated with rabbit brain; (6) the development of an Arthus' phenomenon in guinea-pigs; (7) the presence of circulating antibrain antibodies.

Little is known concerning the antibodies themselves. Little correlation exists between the presence or titre of these antibodies and the development or severity of the encephalitic process. The results of numerous investigations on the presumable antigen are incomplete, but it is apparent that the antigen is related to myelin. The subsequent reaction between antigen and antibody upon the brain is particularly on myelin with the production of extensive and multiple lesions in the central nervous system.

The corollaries that may be drawn with reference to neuroparalytic accidents in man following antirabies vaccination are: (1) this procedure consists of the repeated subcutaneous injections of heterologous brain tissue; (2) the more numerous the injections the higher the percentage of neuroparalytic action; (3) the clinical manifestations of neuritis, myelitis, and encephalitis have their counterpart in experimental encephalitis; (4) the symptoms develop after an incubation period similar to that seen in the experimental animal.

The pathologic findings cannot be differentiated from those observed in allergic encephalomyelitis. The few cases that have been studied with serologic tests show increased brain antibody titres. In addition, antibodies were found in 50 per cent of the individuals who had received a 14 day treatment, and, as in animals, no correlation could be established between the severity of the neurologic manifestations and the antibody titre.

The authors conclude that the experimental allergic encephalitis in animals and neuroparalytic accidents occurring in man following antirabies vaccination are apparently identical conditions. A similar type of allergic encephalitis occurs in dogs and in mice following antirabies vaccination. Two alternates to eliminate the neuroparalytic accidents would be the use of antirabies vaccine that does not contain brain tissue, or the elimination of the encephalitogenic factor from the vaccine. —*Jerry A. Stirman, M.D.*

The Treatment of Tetanus; Role of the Anesthetist. PATRICK SHACKELTON. *Lancet*, Lond., 1954, 2: 155.

IN AN INTERESTING FASHION, the author develops the present-day principles in the treatment of tetanus, from the background of medieval medicine through the use of arrow poison by the Indian tribes of the Amazon, to rhythmic inflation of lungs by Paracelsus. There is a description of the method of transmission and fixation of the neurotoxin from the site of infection to the ventral horn cells of the spinal cord, the introduction of antitoxin, and the development of modern muscle relaxants.

Established cases of tetanus are usually divided into three groups; (1) mild cases, usually with a long incubation period, which will probably recover; (2) severe cases with a short incubation and onset period in patients who will almost certainly die; and (3) cases in which the issue is in doubt. Death from tetanus has usually been due to respiratory causes such as mechanical obstruction from secretion, spasm leading to asphyxia, exhaustion associated with prolonged and recurrent anoxia, and later the pulmonary complications of atelectasis or infection. The many case reports published between 1939 and 1951 do not suggest that the advent of muscle relaxants has greatly increased the chances of survival of patients in groups 2 and 3; and despite the use of the Drinker apparatus or other respirators, if the spasms did not kill the patient the induced paralysis usually did.

Experience in the treatment of poliomyelitis has been found of value in the treatment of patients with tetanus. Ibsen, in 1954, found that patients, even when apparently adequately oxygenated with pure oxygen, died in tank respirators from apparently inadequate elimination of carbon dioxide. Pulmonary secretions and bronchospasm made the respirator ineffective. Tracheotomy and positive pressure inflations through the tracheotomy tube made adequate ventilation possible and aspiration through the tracheotomy tube removed secretions and prevented lethal atelectasis from developing. Once the patient's chest was wet the respirator became increasingly inefficient and even dry cases put into the respirator usually became wet. The key notes of the success of Ibsen and Lassen in reducing the mortality among patients with poliomyelitis with respiratory paralysis were tracheotomy as soon as respiratory involvement seemed probable, positive pressure ventilation with oxygen and, in their cases, nitrogen as an inert gas, with removal of secretions by aspiration via the tracheotomy tube and by postural drainage. Additional measures were the maintenance of fluid and electrolyte balance, nutrition, and the administration of antibiotics.

It is the author's contention that the lessons taught in the treatment of bulbar paralysis can be applied to severe tetanus, and what must be done is to convert the tetanus into a reversible bulbar poliomyelitis and follow the treatment used by Ibsen and Lassen. In the author's opinion the treatment of established tetanus falls under five headings: (1) prevention of the absorption of further toxin by the giving of antitoxin and by surgery of the wound; (2) control of reflex spasm; (3) prevention of intercurrent pulmonary infection; (4) control of fluid and electrolyte balance; and (5) maintenance of strength. In the second, third, and possibly the fourth items, the anesthetist has a part to play for which his general and special training peculiarly fit him. Mephenesin is thought to be the drug of choice in cases with marked spasm. Nitrous oxide in small amounts is thought to be satisfactory to permit a reduction in dosage of centrally depressing sedation —*Allan D. Callow, M.D.*

Antiserum in the Prophylaxis of Rabies. KARL HABEL. *Bull. World Health Org.*, 1954, 10: 781.

RABIES should be one of the ideal diseases in which to use preventive antiserum. Due to the knowledge of the exact time and location of the exposure, the applicability of local injection of antiserum and the long incubation period would indicate that antiserum prophylaxis would be effective. The absence of a definite viremia stage in the pathogenesis of this disease is the only theoretical objection against the use of serum in rabies. Previous workers utilizing antiserum as a means of prophylaxis of rabies have obtained varying results, from no protection to complete protection. However, in this laboratory consistently good results in experimental animals ranging from mice to monkeys have been obtained.

Rabies was induced in experimental animals by the intramuscular injection of street virus into both masseter muscles in the guinea-pig. Studies were performed to compare the effectiveness of serum alone, vaccine alone, and serum plus vaccine in the prophylaxis of rabies. The results of varying the interval time from the virus injections to treatment were compared. The results indicate that serum alone was more effective than vaccine alone. The combination of

serum and vaccine was more effective than either alone. There was some indication that the local administration of serum, followed in 4 days by a vaccine, was slightly more effective than the combined treatment on the same day. Serum given within 3 days after injury decreased the mortality, and, when given at 24 and 48 days tended to prolong the incubation period.

Substantiation for the local injection of antiserum was obtained by comparison of the treatment with normal serum given intramuscularly. It was found that the local injection of antiserum protected against all virus dilutions tested. The authors found that after the local injection of the rabies virus, it could be demonstrated up to 72 hours in the muscle at the site of the original inoculation. By 72 hours the virus was found also in the peripheral nerves and occasionally in the spinal cord.

The combined use of the antiserum and antigen has been questioned because of the interference with the immunizing capacity of the antigen. The experimental data would indicate that if serum were followed by vaccine at an interval of 6 days, the results were slightly better than if it were given concomitantly with the serum. However, other workers were unable to demonstrate any appreciable difference in 1 and 6 day intervals between the two prophylactic treatments. Another worker introduced a street virus intramuscularly in hamsters and followed this by varying dilutions of antiserum given subcutaneously 24 hours later. At an interval of 5 months the survivors from this original experiment were reinoculated intramuscularly with a more severe street virus challenge.

The results of this study indicated that with more concentrated antiserum administered within 24 hours fewer animals succumbed to the original challenge, but on subsequent challenge the survivors were susceptible. With intermediate dilutions of antibody there was less initial protection, but excellent protection, on rechallenge. Similarly, those receiving so little antibody that a few survived the original challenge were also resistant to rechallenge. When the amount of antibody is reduced to the point at which the original challenge breaks through and causes some deaths from rabies, the survivors have a sufficient virus multiplication and antigenic stimulus for subsequent active immunity.

It would appear from these studies that the chief value of antirabies serum would be the prolongation of the incubation time, so that the animal could be observed until definite evidence of rabies was present, or, if the bite was in such a position that a short incubation period would be expected without antiserum, that the prolongation of the incubation period allow the corrective immunization to become effective.

Antiserum, to be effective, should be placed in the local wound if practicable, and should be administered within 72 hours after exposure. In the United States a single dose of concentrated antiserum (produced in horses) in the dose of 0.5 ml. per kgm. of body weight, followed by 14 daily doses of vaccine for severe exposure, is currently becoming available.

—Jerry A. Stirman, M.D.

Clinical Evaluation of Topical Antibiotic Therapy. Alfred J. Suraci. *Plastic & Reconstr. Surg.*, 1954, 14: 89.

Clinical data are presented on the use of two topical dosage forms of aureomycin: (1) a packing gauze impregnated with aureomycin hydrochloride, and (2) a dressing of mesh surgical gauze impregnated with the same drug in a special ointment base. The clinical material includes over 630 cases and almost 1,300 operative sites.

There has never been any evidence of local irritation or allergic response due to the use of these dressing and packing units. In many cases in which local infection had been present, the infection disappeared following the local treatment, in spite of resistance or relative resistance to systemic aureomycin. This fact is probably due to the high local concentration level of aureomycin attainable through the suitable topical applications.

All donor sites appeared cleaner and healed more rapidly. Dressings did not have the tendency to adhere to the wound created by the removal of the skin graft, and the donor site areas were less tender.

There is a distinct advantage to the size of the dressings used—8″ by 12″, 44 x 36 mesh—for they cover sufficient surface, and save work and time when large areas need dressing.

When the aureomycin packing is used daily on malodorous wounds, or every second day, there is prompt improvement in appearance and a decrease or disappearance of the odor. This is of value, particularly in ulcerations due to carcinoma, since the patient is more comfortable. When incision and drainage of abscesses are necessary, the use of aureomycin packing has a prompt effect in cleaning the cavity and hastening healing.

The use of topical antibiotics does not lessen the importance of good surgical technique. In order to attain its full benefits, wounds must be adequately débrided and kept free of detritus. On suppurating wounds, the topical dressing should be changed often and the wound cleansed by washing. Full antibacterial effect cannot be achieved when, due to pus or detritus, the antibacterial agent cannot come in contact with the healing tissue.

—Samuel Kahn, M.D.

ANESTHESIA

The Overuse of Carbon Dioxide Absorption in General Anesthesia. W. N. Kemp. *Am. J. Surg.*, 1954, 87: 864.

The majority of present-day anesthetists take the view that carbon dioxide is a poisonous gas that should be immediately and completely removed from the gases respired by a surgical patient. This is readily accomplished with soda lime. The author is in diametric opposition to this view.

He believes a certain minimal tension of carbon dioxide must be present in the arterial blood for the normal release of oxygen from oxyhemoglobin. He also notes that regulation and depth of respiration is largely controlled by the action of carbon dioxide in a quantitative manner upon the respiratory center. The author suggests that convulsions seen under deep

ether anesthesia are due to hypoxia of the cerebral cortex induced by excessive loss or removal of carbon dioxide from the arterial blood.

The author concluded that quantities of carbon dioxide should be allowed to accumulate in the rebreathing bags of gas machines to approximately 3 per cent of the respired gases in the interests of maintaining a normal Bohr effect in oxygen metabolism and tissue respiration, and for the purpose of maintaining near normal pulmonary ventilation.

—Ely Elliott Lazarus, M.D.

Automatic Electroencephalographic Control of Thiopental Anesthesia. DONALD K. KIERSEY, ALBERT FAULCONER, JR., and REGINALD G. BICKFORD. *Anesthesiology*, 1954, 15: 356.

A LOGICAL SEQUENCE to the development of automatically controlled anesthesia with ether is the extension of the clinical investigation to include pentothal sodium anesthesia.

An apparatus was designed and built that is suitable for the automatic administration of pentothal sodium during surgical procedures. It differs from the machine used in ether anesthesia chiefly in the fact that it contains a filter circuit which limits the cerebral potentials used for automatic control to a narrow band which is outside the range of electric disturbance. The advantages to be gained with this technique are demonstrated.

The behavior of the apparatus during use of *d*-tubocurarine chloride together with pentothal sodium was found to be the same as it was when pentothal sodium was used alone.

The Risk of Anesthesia in Thoracic Surgery (Le risque anesthésique en chirurgie thoracique). HENRI LE BRIGAND, ODETTE LEFEBVRE DE HERRERA, and JACQUELINE LEQUESNE-DELAFONTAINE). *Presse méd.*, 1954. 62: 933.

AMONG 1,115 patients anesthetized for thoracic surgery, complications developed in 28. Ten patients had a difficult anesthetic recovery; 5 had edema of the glottis; 3 had serious laryngospasm; 2 suffered cardiac arrest; and 8 developed anoxia during the recovery period.

Important points in the technique of anesthesia used by the authors for patients with thoracic diseases are as follows: (1) light preoperative medication; (2) topical anesthesia for the pharyngolarynx; (3) induction with pentothal and curare; (4) use of a short and wide intratracheal tube; (5) use of a semi-open circuit which permits better elimination of carbon dioxide than does a carbon dioxide absorber; (6) maintenance of controlled artificial respiration; (7) maintenance of anesthesia with 50 per cent N_2O-O_2 mixture supplemented with small doses of curare, pentothal, and cyclopropane; (8) occasional use of controlled hypotension (in 44 cases out of 1,115); and (9) adequate blood replacement.

Surgery with the thorax open in the lateral decubitus position is productive of respiratory acidosis. Controlled respiration assures filling of the alveoli but accentuates retention of carbon dioxide. The anesthetic eliminates the reflex effect of this retention on the respiratory center. Therefore the concentration of carbon dioxide in the circuit must be kept low.

—Frederick W. Preston, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Some Factors which Affect the Value of Carotid Angiography in the Diagnosis of Brain Tumor. ERNEST H. WOOD. *Am. J. Roentg.*, 1954, 71: 952.

THE AUTHOR reviews 100 cases of verified brain tumors in which cerebral angiography had been performed in an attempt to determine when the procedure was most informative. The evidence indicated that the procedure was rewarding when: (a) the pineal body was obviously displaced (anterior displacement excepted); (b) the lesion seemed localized close to the optic chiasm rather than the optic radiations; (c) the neurologic findings did not point to deep centrally located tumors or tumors in the posterior fossa.

Cerebral angiography localized the lesion in 81 per cent of the patients; its failures seemed the result of anatomic limitations rather than deficiencies in the technique. —*Philip J. Hodes, M.D.*

The Study of Mitral Regurgitation by Roentgen Kymography, with Observations on the Movement of Cardiac Calcifications. VICTOR A. MCKUSICK. *Am. J. Roentg.*, 1954, 71: 961.

THE author describes the roentgen kymographic demonstration of the left atrial expansion during ventricular systole in mitral insufficiency. The kymographic findings are not always in agreement with the conclusions drawn from other methods of evaluating mitral disease or with the operative findings. The kymographic examination, while not completely reliable, may add worth-while information in some cases. Roentgen kymograms are also shown to be of value in demonstrating intracardiac calcifications.
—*L. Adele Kynette, M.D.*

The Roentgen Diagnosis of Polycystic Kidneys. LARS BILLING. *Acta radiol.*, Stockh., 1954, 41: 305.

ALTHOUGH the roentgen diagnosis of polycystic kidneys is relatively easy in the advanced stages of the disease, considerable difficulty may be encountered in the early stage when a differentiation is desired between this condition and the normal and pathologic variations in the shape and size of the kidney and pelvis. With this view in mind, the author studied the roentgen findings in 14 patients examined during the last 4 years at Sahlgrenska Sjukhuset, in whom the diagnosis of polycystic kidneys was confirmed by operation, aortography, or typical urographic findings. For the purpose of comparison, the urograms of 50 patients with normal kidneys were also reviewed.

Ten roentgen signs were found to possess clinical value in arriving at the diagnosis of polycystic kidneys. They may be divided into three groups: (a) changes in the outline of the kidney; (b) changes in the contrast-filled pelvis, as demonstrated by urography or retrograde pyelography, and (c) changes seen in aortography. The incidence of these signs in the pathologic and normal kidneys and their relationship to the three subgroups is shown in Table I.

TABLE I

Group of signs	*No.*		*27 Polycystic kidneys*					*100 Normal kidneys*
			+	−	?	0	%+	%+
a	1	Length of the kidney > 14 cm.	27	0	0	0	100	1
	2	Embossed, polycyclic outline	3		24		11	1
	3	Thickness of the parenchyma > 3 cm	25	1	0	1	93	0
	4	Length of the pelvis > 9 cm	21	5	1	0	78	1
	5	Elongation of a calyx	17	8	1	1	63	4
	6	Multiple cyst impressions in the pelvis	24	1	1	1	89	0
b	7	Lateral position of the pelvis	3	23	0	1	11	2
	8	Long axis of the pelvis parallel to the spine	17	9	0	1	63	3
	9	Horn-shaped pelvic ampulla (a & b).	20	5	0	2	74	20
		a. Horizontal horn	9				33	1
		b. Oblique horn.	11				41	19
c	10	Worm-eaten cortex in the aortographic nephrogram	8	—	—	—	—	—

\+ = Sign positive.
— = Sign negative.
? = Impossible to judge if positive or negative.
0 = Not determined: insufficient distinguishable outlines or incomplete contrast filling of the pelvis.

As may be seen from the table, only signs 3, 6, and 10 are of decisive importance from the point of view of differential diagnosis; however, in cases with indistinct outlines and incomplete contrast-filling of the pelvis, every sign may acquire some value in aiding one to recognize the nature of the lesion. It is quite possible that additional experience with signs 1–9 may obviate the necessity of aortography, although in the doubtful case successful aortography is always a deciding factor in establishing the correct diagnosis.
—*T. Leucutia, M.D.*

Calcification of the Intervertebral Discs in Childhood. FREDERIC N. SILVERMAN. *Radiology*, 1954, 62: 801.

CALCIFICATION of the intervertebral discs in children is exceedingly rare. A careful review of the literature reveals that only 8 such cases have been recorded. The author now contributes 7 additional cases. On the basis of the available data in all 15 cases he tries to evaluate the clinical significance of the calcification. It is his opinion that the condition is more common than the cited series of cases would lead us to believe.

After a description of the structure of the intervertebral discs and an analysis of the literature as regards the occurrence of calcification of the intervertebral discs in adults, he presents a detailed account of the 7 personal cases by including roentgenographic repro-

ductions for illustration of the salient points. He then summarizes, in a comprehensive table, the clinical and roentgenographic findings in these cases, as well as in the 8 cases found in the literature.

Recognizing that the distinction is not clear-cut, the author is tempted to divide the patients into two groups: (a) those with acute symptoms of pain and fever, and transient calcification, most commonly in the cervical region; and (b) those with "permanent" calcification, generally thoracic or lumbar, unassociated with recognizable symptoms. He states that neither age, nor location, nor the duration of the calcification are valid criteria for evaluating the nature of the process. The factors accounting for the appearance, persistence, or disappearance of the calcification are likewise unknown.

Obviously, additional reports must be awaited before more light can be thrown on the subject. The author feels that because of this, the institution of intensive treatment in the presence of symptoms referable to the level of calcification is not justified.

—*T. Leucutia, M.D.*

The Value of Radiation Therapy in the Management of Intrinsic Tumors of the Spinal Cord. Ernest H. Wood, Alfred S. Berne, and Juan M. Taveras. *Radiology*, 1954, 63: 11.

The case histories of 62 patients with verified intrinsic tumors of the spinal cord were studied. These tumors were divided into four groups: ependymomas, astrocytomas, miscellaneous tumors, and unclassified. The average age of the patients was 37 years.

Pathologic verification was obtained in 39 cases, and verification in the other 23 cases was obtained by palpation and inspection. In the pathologically verified group there were 23 ependymomas and 12 astrocytomas. These made up the major tumor group.

Postsurgical irradiation therapy was given to the entire 62 patients with the usual deep therapy apparatus (200 kv., HVL 1 mm. of copper). The patients were treated by individual methods but the average tumor dose was 1,700 roentgens in a 14 day period. Retreatment was instituted when clinically indicated.

The survival period was compared with that obtained by Woltman (*Arch. Neurol. Psychiat.*, 1944, 52: 383–399) who followed 34 such patients after only surgical treatment. The average survival period in his group was 6 years.

Of the 36 patients treated prior to 1947 (the 6 year period), 25 patients lived 6 years or longer. So far as the ependymoma group is concerned, 12 of the 16 patients treated prior to 1947 are living.

The authors believe that the radiation therapy invariably alleviates pain, helps restore function frequently, and inhibits the progression of disability. They recommend, as a result of these studies, a conservative surgical approach to spinal cord tumors, followed by radiation therapy.

—*John J. Gaughan, M.D.*

MISCELLANEOUS

The Vaginal Smear as a Prognostic Aid in Carcinoma of the Cervix Treated According to the Individualized Stockholm Method. Gertrude Kohn. *Acta radiol.*, Stockh., 1954, 41: 446.

In 1947 Graham published a 5-year survival report on a group of patients in whom the cytologic changes in the benign vaginal cells had been observed during radiation treatment for carcinoma of the cervix. Of 37 patients showing only little cytologic change during radiotherapy, only 1 was alive at 5 years, whereas of 36 patients showing marked changes, 20 were alive at 5 years.

In an attempt to duplicate this work, vaginal smears were taken once weekly throughout treatment of 45 patients with histologically verified carcinoma of the cervix, and in an additional 5 cases smears were obtained on single occasions, 3 to 4 weeks after the first and second radium treatments.

Of the total number of 50 patients, 32 were recorded as having a "good response" (the benign vaginal cells showed definite evidence of the radiation effect), and of these 32 patients only 5 had persistent disease or recurrence within the follow-up period of 1 to 1½ years.

Poor response was recorded in 18 cases and of these, 16 had recurrent or persistent disease.

Although the period of observation in these cases has been short, the findings suggest that the vaginal smears taken during radiotherapy, a simple and safe procedure, may prove to be a reliable index of prognosis in carcinoma of the cervix. In this series, if a "good" response was not apparent after the first radium application, the response did not change after the second application. —*Lois Cowan Collins, M.D.*

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

ABO Blood Groups and the Toxemia of Pregnancy. L. A. Pike and A. M. Dickins. *Brit. M. J.*, 1954, 2: 321.

The distribution of blood groups among 3,651 admissions to a maternity hospital has been studied. These admissions included 541 patients who were suffering from toxemia of pregnancy. As compared with the nontoxemic patients, the toxemic patients showed a significant excess of women of group O.
—*Ernest D. Bloomenthal, M.D.*

The Pathogenic Etiology of Occupational Tumors (Considerazioni sulla eziopatogenesi delle neoplasie professionali). G. Di Macco. *Boll. oncol.*, Rome, 1954, 28: 27.

The present discussion deals with the hereditary and acquired predisposing factors that have been observed in occupational neoplasms.

The carcinogenic stimulus is characterized by chronicity and aspecificity. A variety of stimuli (physical, chemical, or biological) acting for different intervals over a long period of time have been capable of producing carcinogenic lesions. In this respect the lesions differ from other recognized entities such as infections and inflammations. The combined effect of these various stimuli must also be accounted for in etiological explanations. In attempting to combine the above factors, the author presents arguments to support the congenital and acquired hereditary factors as being the important strata to explain the development of neoplastic lesions.

The argument is supported by observations on experimentally produced adenocarcinoma of the breast in albino rats. In these offspring, carcinomatous lesions can be produced by the prolonged administration of estrogens; they can also be prevented by castration. A virus factor present in these strains of mice will not produce cancer in unbred mice. This latter factor is said to be transmitted by the breast milk of susceptible rats. Thus, there are a variety of factors acting over a prolonged period of time. Obviously, the most important factor is the experimental transmission of the hereditary factors by genetic transfer.

The purpose in presenting this argument is to explain the etiology of scrotal cancer in chimney sweepers, and the cause of mucosal leucoplakia and intestinal carcinomas. —*Roland A. Manfredi, M.D.*

Malignant Transformation of Squamous Epithelium; a Cytochemical Study with Special Reference to Cytoplasmic Nucleic Acids and Proteins. Gunnar Moberger. *Acta radiol.*, Stockh., 1954, supp. 112.

The author made cytochemical analyses of squamous epithelium, using the absorption of radiant energy for the purpose of comparing the dry weight and the nucleic acid distribution in squamous epithelium at varied stages of malignant transformation. He gave details as to why squamous epithelium was selected and also presented advantages of the freeze-drying technique in preserving the tissues which are to be analyzed. Many of the various methods of conducting these determinations are elaborated. His conclusions were the same on the basis of the different methods, both with experimental animals and with clinical material.

There are diagrams and photographs of the equipment, graphs, and tables to supplement the written data. —*Mark T. Wheelock, M.D.*

Blood Groups in Carcinoma of the Lung. R. B. McConnell, C. A. Clarke, and F. Downton. *Brit. M. J.*, 1954, 2: 323.

The blood groups represented in 777 histologically proved cases of carcinoma of the lung in one hospital are compared with those of 1,000 blood donors in the same area. No significant or near significant difference is found in the ABO distribution of the two series.

On breakdown into histologic subdivisions, an excess of group A at the expense of group O is found in the oat-cell tumors, but not in the other types which have a normal ABO distribution.

Among 555 cases tested with anti-D serum, 12.43 per cent were Rhesus-negative; when compared with the control figure of 18.4 per cent Rhesus-negative, this is statistically significant. The deficiency of Rhesus-negative applied particularly to the 251 squamous-cell carcinomas. —*Ernest D. Bloomenthal, M.D.*

The Blood Groups in Relation to Peptic Ulceration and Carcinoma of Colon, Rectum, Breast, and Bronchus; an Association Between the ABO Groups and Peptic Ulceration. Ian Aird, H. H. Bentall, J. A. Mehigan, and J. A. Fraser Roberts. *Brit. M. J.*, 1954, 2: 315.

Data are presented on the ABO blood-group frequencies among 3,011 patients with peptic ulcer, mainly those who have required treatment by transfusion and/or operation, 2,599 with cancer of the colon and rectum, 998 with cancer of the bronchus, and 1,017 with cancer of the breast.

Compared with controls from the general population of the areas sampled, patients suffering from peptic ulcer show an increased incidence of group O and a correspondingly lower incidence of the other three groups. The difference is a large one as it appears that persons of group O are about 35 per cent more likely to develop peptic ulceration than are persons of the other groups.

The ABO frequencies shown by the three cancers do not differ significantly from the population controls. These three negative results serve as a test of the appropriateness of using population controls for hospital patients. On the numbers available, there is no indication of any difference in ABO frequencies between gastric and duodenal ulcer.

In none of the diseases is there any significant difference in sex proportion or in age between patients

of the four blood groups. Patients suffering from the four diseases do not differ significantly in the proportion who are Rhesus-negative, the overall value being close to the expectation in the general population.

—Ernest D. Bloomenthal, M.D.

The Causal Relationship Between Benign Epithelial Tumors and Adenocarcinoma of the Colon and Rectum. K. A. HULTBORN. *Acta radiol.*, Stockh., 1954, supp. 113.

IN this study, the author elaborates on much of the work of a similar nature which has been done in the United States and elsewhere on the relationship of the "benign polyp" to adenocarcinoma of the colon. He believes that benign polyps in the distal colon and rectum which are within reach of the sigmoidoscope should be treated as potential carcinomas. He is convinced that those in the proximal colon are sufficiently apt to become malignant to justify the diagnosis of a malignant condition or examination by other means. He is not assured of the true value of the health check as a routine procedure in asymptomatic persons. It is necessary to determine by sigmoidoscopic examination the presence of a "polyp".

The presentation is in three parts: The written data, case summaries, and photographs.

—Mark T. Wheelock, M.D.

Development of Sarcoma After Trauma (Sarkomentstehung nach Verwundung). GEORG EBERT. *Langenbecks Arch. u. Deut. Zschr. Chir.*, 1954, 278: 218.

THE AUTHOR, of the Surgical Department of the University of Goettingen, Germany, discusses the theories concerning the connection between bone injury and sarcoma and describes 3 pertinent cases of his own observation.

In the first 2 cases a fibrosarcoma developed 8 and 10 years, respectively, after a shell fragment injury of the humerus in one case and of the femur in the other case. The author raises the question whether the embedded shell fragments exerted a chronic chemical irritation of the soft tissues, and quotes clinical experiences as well as animal experiments which indicated that chronic exposure to metals (iron, nickel) may predispose to the development of malignancies.

In the third case a sarcoma developed in the stump of an amputated femur 37 years after the amputation. The question whether chronic pressure of the prosthesis was responsible for the development of the tumor cannot be definitely decided. However, the author answers the question in the affirmative, especially since a neuroma had developed in the stump years prior to the sarcoma.

—Werner M. Solmitz, M.D.

EXPERIMENTAL SURGERY

Tolerance of Adult Rats to Profound Hypothermia and Simultaneous Cardiac Standstill. SUAD A. NIAZI and F. JOHN LEWIS. *Surgery*, 1954, 36: 25.

RECENT WORK has indicated the feasibility of using moderate hypothermia to permit total circulatory interruption for brief periods, thus providing a bloodless field for intracardiac surgery. This experiment with rats was conducted to see if a more profound hypothermia might be induced, and hence a longer period of circulatory arrest permitted, and still have survival of the animal.

Previous experiments have indicated that rats were unable to survive hypothermia below 15° C. In this series 47 anesthetized rats were cooled to 8.5° C. or below, with artificial respiration being given during the cooling and re-warming periods. Cardiac arrest occurred in all animals. During re-warming, cardiac action resumed at temperatures of from 4.5° C. to 14° C. Artificial respiration was continued until spontaneous respirations began at 25° to 30° C. In 3 to 5 hours, the animals were able to crawl and climb. Animals with cardiac arrest for more than 1 hour, had 2 or 3 days of some flaccid paralysis of the hind limbs following re-warming.

Of 12 rats in whom cardiac arrest was maintained for 35 to 44 minutes, 7 lived from 1 to 8 days before dying of respiratory obstruction and the remaining 5 were still alive at 13 to 16 weeks.

Of 21 rats with cardiac arrest for 1 hour to 3 hours, 13 survived the hypothermia. Of these, 12 died in from 1 hour to 7 days, and 1 was still living at 16 weeks.

Fourteen animals were in cardiac arrest for 13 to 16 hours, with 4 of these surviving up to 5 hours.

Compared to the previous reports of death following hypothermia and cardiac arrest in rats, the survival of animals in this report is attributed to administration of artificial respiration, particularly during the cooling period. *—Stanley W. Tuell, M D.*